2: Am J Respir Crit Care Med 2000 Sep;162(3 Pt 1):1175-7

Exhaled 8-isoprostane as an in vivo biomarker of lung oxidative stress in patients with COPD and healthy smokers.

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Imperial College School of Medicine at the National Heart and Lung Institute, Department of Thoracic Medicine, London, United Kingdom.

Most of the studies linking chronic obstructive pulmonary disease (COPD) with oxidative stress are in vitro, using invasive techniques, or measuring systemic oxidative stress. The aim of this study was to quantify oxidative stress in the lungs in patients with COPD and in healthy smokers, as reflected by 8-isoprostane concentrations in breath condensate. This is a noninvasive method to collect airway secretions. 8-Isoprostane is a **prostaglandin-F(2alpha)** isomer that is formed in vivo by free radical-catalyzed peroxidation of arachidonic acid. We also studied the acute effect of **smoking** on exhaled 8-isoprostane in healthy smokers. Exhaled 8-isoprostane was measured by a specific enzyme immunoassay in 10 healthy nonsmokers and 12 smokers, 25 COPD ex-smokers, and 15 COPD current smokers. 8-Isoprostane concentrations were similar in COPD ex-smokers (40 +/- 3.1 pg/ml) and current smokers (45 +/- 3.6 pg/ ml) and were increased about 1.8-fold compared with healthy smokers (24 +/- 2.6 pg/ml, $p < 0.001$), who had 2.2-fold higher 8-isoprostane than healthy nonsmokers (10.8 +/- 0.8 pg/ml, $p < 0.05$). **Smoking** caused an acute increase in exhaled 8-isoprostane by about 50%. Our study shows that free radical production is increased in patients with COPD and that **smoking** causes an acute increase in oxidative stress.

PM3000457309

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

3: Clin Pharmacol Ther 2000 Aug;68(2):167-74

Transdermal nicotine mimics the smoking-induced endothelial dysfunction.

Sabha M, Tanus-Santos JE, Toledo JC, Cittadino M, Rocha JC, Moreno H Jr

Department of Pharmacology, Faculty of Medical Sciences, State University of Campinas, Sao Paulo, Brazil.

BACKGROUND: Cigarette **smoking** is a major risk factor for coronary artery disease and causes endothelial dysfunction, perhaps by decreasing the availability of nitric oxide availability in arteries and veins. Nicotine in cigarette smoke may be responsible for this impaired endothelial response. METHODS: We studied nine healthy nonsmokers and 12 healthy mild to moderate smokers by use of the dorsal hand vein compliance technique. Dose-response curves to bradykinin and sodium nitroprusside were obtained to test the endothelium-dependent and endothelium-independent vasorelaxation before and during the use of a nicotine (21 mg) patch. Mean arterial blood pressure and heart rate were measured beat-to-beat during the 4-hour study and serial blood samples were drawn to assay plasma thromboxane B2 levels. RESULTS: Transdermal nicotine reduced the venous responsiveness to bradykinin in nonsmokers (Emax = 88.0% +/- 17.9% and 54.3% +/- 14.9%, respectively, before and after the nicotine patch; P < .05); the latter response was similar to that in smokers (Emax = 56.3% +/- 16.6%). Sodium nitroprusside-induced venodilation was unaltered. Mean arterial blood pressure increased in both smokers and nonsmokers. Transdermal nicotine increased the plasma **thromboxane B2** concentrations only among nonsmokers. CONCLUSION: These findings indicate that nicotine can have a major role in the impaired endothelial function in smokers. The results probably also reflect what occurs in arterial beds because the nicotine patches increased the mean arterial blood pressure in both smokers and nonsmokers.

Publication Types:
Clinical trial
Controlled clinical trial

PM3000457310

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

4: Prev Med 2000 Aug;31(2 Pt 1):148-52

Effects of the transdermal nicotine patch on normalization of HDL-C and its subfractions.

Moffatt RJ, Biggerstaff KD, Stamford BA

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BACKGROUND: **Smoking** reduces **HDL**-C and its subfractions, and **smoking** cessation leads to normalization of these lipoproteins. Nicotine replacement therapy is an important weapon employed by those attempting to quit **smoking**. This study examined the effects of the transdermal nicotine patch ("patch") on lipoproteins. METHODS: Ten male and 17 female smokers refrained from **smoking** for 77 days. The patch was utilized during the first 35 days and then removed for the remaining 42 days. Seven male and 9 female nonsmokers were controls. RESULTS: **HDL-C, HDL(2)-C, and HDL(3)-C** levels were significantly lower in smokers when compared with controls. These differences were sustained during the initial 35 days when using the patch. Over the following 42 days, however, these lipoproteins normalized to values similar to those of control subjects. Females who quit **smoking** gained 2.1 kg after the patch was removed. CONCLUSIONS: It was concluded that nicotine as administered by the transdermal nicotine patch inhibits normalization of **HDL**-C, **HDL**(2)-C, and **HDL**(3)-C in those who have quit **smoking**. Removal of the patch results in normalization of these lipoproteins. The patch appeared to prevent weight gain among female subjects. Copyright 2000
American Health Foundation and Academic Press.

Publication Types:
Clinical trial
Randomized controlled trial

PM3000457311

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

5: Chem Biol Interact 2000 Jul 3;127(2):125-37

Autoantibody against oxidized low-density lipoproteins may be enhanced by cigarette smoking.

Liu CS, Lii CK, Ou CC, Tsai CH, Wei YH, Chen HW

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A total of 59 healthy male subjects (32 smokers and 27 nonsmokers) who had no reported systemic disease and did not take alcohol and vitamin supplementation were included. The levels of autoantibody to oxidized low-density lipoproteins (**ox-LDL**) in smokers and age-matched nonsmokers were compared. The plasma levels of antioxidants that can affect the formation of ox-**LDL** were also measured, and correlation analyses between anti ox-**LDL** IgG and plasma antioxidants, controlling for age and body mass index (BMI), were performed. Plasma alpha-tocopherol and uric acid concentrations of nonsmokers (2.78+/-1.09 microg/mg total lipid and 6.96+/-1.69 mg/dl, respectively) were significantly higher than those of smokers (1.68+/-0.48 microg/mg total lipid and 6.15+/-1.14 mg/dl, respectively) (P<0.05). Although plasma ascorbate and retinol levels were not significantly different between smokers and nonsmokers, smokers older than 45 years old had significantly lower plasma ascorbate levels (0.32+/-0.17 mg/dl) than age-matched nonsmokers (0. 53+/-0.14 mg/dl) (P=0.036). Higher level of plasma anti **ox-LDL** IgG was noted in the group of smokers compared with nonsmokers (515+/-409 mU/ml vs. 407+/-268 mU/ml, respectively) under the statistic method of Chi-Square test (P=0.049). A significant negative correlation was found between plasma anti ox-**LDL** IgG and alpha-tocopherol in the combined population as well as in the smoker group (r=-0.26, p=0.047; r=-0.48, p=0.006; respectively). However, there was no correlation between plasma anti ox-**LDL** IgG and the levels of other antioxidants. These results suggest that reduced concentrations of alpha-tocopherol are associated with cigarette **smoking**. The significantly negative correlation between plasma anti **ox-LDL** IgG and alpha-tocopherol in the entire study population as well as in the smoker group suggests that plasma alpha-tocopherol may be partially effective if not totally at protecting **LDL** from oxidative damage caused by cigarette **smoking** and dietary supplementation with alpha-tocopherol may provide a protective effect against **LDL** oxidation, especially in smokers.

PM3000457312

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

6: Circulation 2000 Aug 1;102(5):539-45

Effects of vitamin E supplementation on F(2)-isoprostane and thromboxane biosynthesis in healthy cigarette smokers.

Patrignani P, Panara MR, Tacconelli S, Seta F, Bucciarelli T, Ciabattoni G, Alessandrini P, Mezzetti A, Santini G, Sciulli MG, Cipollone F, Davi G, Gallina P, Bon GB, Patrono C

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BACKGROUND: Increased formation of **8-iso-prostaglandin (PG) F(2alpha)** and thromboxane (TX) A(2), potent agonists of platelet and vascular thromboxane (TH)/PGH(2) receptors, has been detected in cigarette smokers. We performed a randomized, double-blind, placebo-controlled study of the effects of vitamin E (300, 600, and 1200 mg/d, each dose for 3 consecutive weeks) on **8-iso-PGF(2alpha)** and TXA(2) biosynthesis in 46 moderate cigarette smokers. METHODS AND RESULTS: Urinary immunoreactive **8-iso-PGF(2alpha)** and 11-dehydro-**TXB(2)**, plasma vitamin E, and serum **TXB(2)** were measured by previously validated techniques. Baseline urinary **8-iso-PGF(2alpha)** and 11-dehydro-**TXB(2)** excretion averaged 241+/-78 and 430+/-293 pg/mg creatinine, respectively. Urinary **8-iso-PGF(2alpha)** was significantly correlated with 11-dehydro-**TXB(2)** (r=0.360, n=138, P<0.0001). Baseline plasma vitamin E levels averaged 20.6+/-4.9 micromol/L and were inversely correlated with urinary 11-dehydro-**TXB(2)** (r=-0.304, P=0.039) but not with 8-iso-PGF(2alpha) (r=-0.227, P=0.129). Vitamin E supplementation caused a dose-dependent increase in its plasma levels that reached a plateau at 600 mg (42.3+/-11.2 micromol/L, P<0. 001). This was not associated with any statistically significant change in urinary **8-iso-PGF(2alpha)** or 11-dehydro-**TXB(2)** excretion. CONCLUSIONS: Supplementation with pharmacological doses of vitamin E has no detectable effects on lipid peroxidation and thromboxane biosynthesis in vivo in healthy subjects with a mild degree of oxidant stress. These findings are consistent with the hypothesis that the basal rate of lipid peroxidation is a major determinant of the response to vitamin E supplementation and have implications for the use of vitamin E in healthy subjects as well as for the design and interpretation of clinical trials of antioxidant intervention.

Publication Types:
Clinical trial
Multicenter study
Randomized controlled trial

PM3000457313

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

7: Ann Clin Biochem 2000 May;37 (Pt 3):313-8

LDL subfractions in patients with myocardial infarction: effect of smoking and beta-blocker treatment.

Theodoraki TG, Tsoukatos DC, Karabina SA, Rallidis LS, Papageorgakis NH, Tselepsis AD

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The aim of the present case-control study was to estimate, by density gradient ultracentrifugation, **LDL** heterogeneity in myocardial infarction, and to evaluate the effect of **smoking** and beta-blocker treatment on **LDL** subfraction profile. Our results show that patients who survive myocardial infarction have an abundance of small, dense **LDL** in their plasma, compared with controls. Patients who were on beta-blockers and those who smoked showed a more atherogenic **LDL** subfraction profile than the rest. In patients on beta-blocker treatment, the proportion of **LDL**3 was positively correlated with triglyceride concentration and body mass index. Dense **LDL** predominates in patients irrespective of **smoking** or beta-blocker treatment. The relative risk, calculated by logistic regression as the odds ratio of high **LDL**3, was 7.5 (95% confidence interval 2.5-22.1) and was not significantly influenced when **smoking**, beta-blocker treatment, triglycerides or the other parameters of the study were included in the statistical model.

PM3000457314

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

8: Circulation 2000 May 16;101(19):2252-7

Smoking is associated with reduced serum paraoxonase activity and concentration in patients with coronary artery disease.

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BACKGROUND: Paraoxonase is an **HDL**-associated enzyme that protects lipoproteins from oxidative modifications. **Smoking** is a major cardiovascular risk factor that promotes lipid peroxidation. Cigarette smoke has been shown in vitro to inhibit paraoxonase. The present study examined the hypothesis that **smoking** is associated with modulated serum activities and concentrations of paraoxonase. METHODS AND RESULTS: Coronary artery disease was assessed with the use of coronary arteriography in participants recruited from a hospital cardiology division. Medical and lifestyle data were obtained, and a fasting blood sample was provided. Three **smoking** categories were established (never, ex-smokers, and current smokers), and serum paraoxonase variables were compared among them. The activities and concentrations of paraoxonase were significantly lower in current than in never smokers. Ex-smokers had values comparable to those of never smokers. Ex-smokers who had recently stopped (<3 months) had activities and concentrations comparable to those of current smokers; values returned to the levels of never smokers within 2 years of cessation of **smoking**. **Smoking** status was an independent determinant of paraoxonase activity and concentration in multivariate analysis. Finally, lower paraoxonase was associated with more severe coronary disease and a reduced capacity to protect **LDL** from oxidation. CONCLUSIONS: **Smoking** is independently associated with significant decreases in serum paraoxonase activities and concentrations, which normalize within a relatively short time of cessation. Lower serum paraoxonase is linked to more severe coronary artery disease and a lower antioxidant capacity. The data are consistent with the hypothesis that **smoking** modifies serum paraoxonase such that there is an increased risk of coronary artery disease due to a diminished capacity to protect lipoproteins from oxidative stress.

PM3000457315

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

9: Am J Epidemiol 2000 May 1;151(9):892-901

Prospective study of diet, lifestyle, and intermittent claudication in male smokers.

Tornwall ME, Virtamo J, Haukka JK, Aro A, Albanes D, Huttunen JK

National Public Health Institute, Helsinki, Finland.

The association between dietary and lifestyle factors and intermittent claudication was investigated in the Finnish Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. The cohort comprised 26,872 male smokers aged 50-69 years who were free of claudication at study entry. At baseline (1985-1988), subjects completed a diet history questionnaire. During a median follow-up period of 4 years (ending in spring 1993), 2,578 men reported symptoms of claudication on the Rose questionnaire, which was administered annually. **Smoking** status was assessed every 4 months. **Smoking**, systolic blood pressure, serum total cholesterol, and diabetes mellitus were positively associated with risk for claudication, whereas serum **high density lipoprotein** cholesterol, education, and leisure time exercise were inversely associated with risk. Dietary carbohydrates, fiber, and n-6 polyunsaturated fatty acids were inversely associated with risk for claudication, as were some dietary and serum antioxidants: dietary vitamin C (highest quartile vs. lowest: relative risk (RR) = 0.86; 95% confidence interval (CI): 0.77, 0.97), dietary gamma-tocopherol (RR = 0.89; 95% CI: 0.79, 1.00), dietary carotenoids (RR = 0.82; 95% CI: 0.73, 0.92), serum alpha-tocopherol (RR = 0.88; 95% CI: 0.77, 1.00), and serum beta-carotene (RR = 0.77; 95% CI: 0.68, 0.86). **Smoking** cessation reduced subsequent risk for claudication (RR = 0.86; 95% CI: 0.75, 0.99). The authors conclude that classical risk factors for atherosclerosis are associated with claudication. High intakes of antioxidant vitamins may be protective. Further research is needed before antioxidants can be recommended for the prevention of intermittent claudication.

PM3000457316

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

10: Int J Clin Lab Res 1999;29(4):150-4

The influence of smoking on von Willebrand factor is already manifest in healthy adolescent females: the Floren-teen (Florence Teenager) Study.

Prisco D, Fedi S, Brunelli T, Chiarugi L, Lombardi A, Gianni R, Santoro E, Cappelletti C, Pepe G, Gensini GF, Abbate R

Istituto di Clinica Medica Generale e Cardiologia, University of Florence, Italy.

The early onset of atherosclerosis and the involvement of physiological biochemical, and environmental factors in its pathogenesis is well documented. Few data are available on the role of risk factors related to hemostasis in the pathogenesis of atherosclerosis in the young and, in particular, little information is available on adolescent populations. In the Study of Preventive Medicine and Education Program (Floren-teen Study), von Willebrand factor, a risk factor for cardiovascular disorder, was studied, together with classical cardiovascular risk factors, in apparently healthy students from two high schools in Florence. Familial and personal history, physical examination, and cardiovascular risk factors were evaluated in 144 students (aged 17-19 years). Blood was withdrawn to assess von Willebrand factor (ELISA) and lipid parameters. Levels of von Willebrand factor were significantly higher ($P<0.044$) in smokers than in nonsmokers and were correlated with the number of cigarettes per day in the whole group ($P=0.01$) and in females ($P=0.006$). In females a positive correlation was observed between von Willebrand factor and **high-density lipoprotein** cholesterol ($P=0.0365$). There was no significant correlation between von Willebrand factor and blood pressure or between von Willebrand factor and physical activity. In conclusion, this study shows an association between levels of von Willebrand factor and **smoking** habits and is the first show that even a brief period of **smoking** affects levels of von Willebrand factor in healthy adolescent females independently of other risk factors. These results stress the relevance of extending prevention programs to reduce **smoking** in high school students.

PM3000457317

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

11: Clin Chest Med 2000 Mar;21(1):159-72
Smoking and cardiovascular disease.

Villablanca AC, McDonald JM, Rutledge JC

Department of Internal Medicine, University of California at Davis, School of Medicine, USA.

Mainstream and ETS exposure are strong risk factors for cardiovascular disease in men and women. The relationships between **smoking** and cardiovascular disease result from multiple mechanisms that interact to contribute to atherosclerosis, vascular injury, thrombosis, and vascular dysfunction. We are only now beginning to understand how **smoking** contributes to the genesis and progression of cardiovascular disease. Because of the complexity of the interactions between nicotine and the components of MSS, ETS, and sidestream smoke with the vasculature, it will take a great deal of time and effort to fully unravel the mechanisms by which **smoking** contributes to cardiovascular disease. In addition, cardiovascular risk in female smokers is complicated by hormonal variables that may contribute to greater relative risk. It is important that health care providers, educators, and policy makers recognize the changing patterns of **smoking** and the impact of **smoking** on cardiovascular disease, and continue campaigns aimed at enhancing **smoking** cessation in the general population and in teens. Rigorous research is needed on the changing cultural, psychosocial, and environmental factors that influence tobacco use to improve our understanding of racial/ethnic **smoking** patterns, and identify strategic tobacco control opportunities. The capacity of tobacco control efforts to keep pace with patterns of tobacco use and cessation depends on timely recognition of emerging prevalence and cessation patterns and the resulting development of appropriate community-based programs to address the factors involved. **Smoking** trends today will determine how heavy the health burden of cardiovascular disease and others will be among communities tomorrow. Programs that aim at early intervention and reflect cultural diversity will be the cornerstone in the battle against tobacco use. Continued interest in research, educational, and prevention efforts are needed to help curb the risk of cardiovascular disease from **smoking** in men and women.

Publication Types:
Review
Review, academic

PM3000457318

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

12: J Am Coll Cardiol 2000 Feb;35(2):277-83

Effects of vitamin E on chronic and acute endothelial dysfunction in smokers.

Neunteufl T, Priglinger U, Heher S, Zehetgruber M, Soregi G, Lehr S, Huber K, Maurer G, Weidinger F, Kostner K

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OBJECTIVES: The aims of this study were to determine whether chronic or acute impairment of flow mediated vasodilation (FMD) in the brachial artery of smokers can be restored or preserved by the antioxidant vitamin E. BACKGROUND: Transient impairment of endothelial function after heavy cigarette **smoking** and chronic endothelial dysfunction in smokers result at least in part from increased oxidative stress. METHODS: We studied 22 healthy male smokers (mean +/- SD, 23 +/- 9 cigarettes per day) randomly assigned to receive either 600 IU vitamin E per day (n = 11, age 28 +/- 6 years) or placebo (n = 11, age 27 +/- 6 years) for four weeks and 11 age-matched healthy male nonsmokers. Flow mediated vasodilation and endothelium-independent, nitroglycerin-induced dilation were assessed in the brachial artery using high resolution ultrasound (7.5 MHz) at baseline and after therapy. Subjects stopped **smoking** 2 h before the ultrasound examinations. At the end of the treatment period, a third scan was obtained 20 min after **smoking** a cigarette (0.6 mg nicotine, 7 mg tar) to estimate transient impairment of FMD. RESULTS: Flow mediated vasodilation at baseline was abnormal in the vitamin E (5.3 +/- 3.8, $p < 0.01$) and in the placebo group (6.4 +/- 3.5, $p < 0.05$) compared with non**smoking** controls (11.6 +/- 4.7). Using a two-way repeated measures analysis of variance (ANOVA) to examine the effects of vitamin E on FMD, we found no effect for the grouping factor ($p = 0.5834$) in the ANOVA over time but a highly significant difference with respect to time ($p = 0.0065$).
The interaction of the time factor and the grouping factor also proved to be significant ($p = 0.0318$). Flow mediated vasodilation values remained similar after treatment for four weeks in both groups but declined faster after **smoking** a cigarette in subjects taking placebo compared with those receiving vitamin E (p values from successive differences for the time/group factor: 0.0001/0.0017). The transient attenuation of FMD (calculated as the percent change in FMD) was related to the improvement of the antioxidant status, estimated as percent changes in **thiobarbituric acid-reactive substances** ($r = -0.67$, $p = 0.0024$). Nitroglycerin-induced dilation did not differ between study groups at baseline or after therapy. CONCLUSIONS: These results demonstrate that oral supplementation of vitamin E can attenuate transient impairment of endothelial function after heavy **smoking** due to an improvement of the oxidative status but cannot restore chronic endothelial dysfunction within four weeks in healthy male smokers.

Publication Types:
Clinical trial
Randomized controlled trial

PM3000457319

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

13: Environ Health Perspect 2000 Feb;108(2):105-8

Plasma levels and redox status of ascorbic acid and levels of lipid peroxidation products in active and passive smokers.

Ayaori M, Hisada T, Suzukawa M, Yoshida H, Nishiwaki M, Ito T, Nakajima K, Higashi K, Yonemura A, Ohsuzu F, Ishikawa T, Nakamura H

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Both active and passive **smoking** are regarded as risk factors for various diseases. To clarify the effects of active and passive **smoking** on plasma vitamin C levels and lipid peroxidation status, we examined the plasma levels of ascorbic acid (AA), its redox status [ratio of dehydroascorbate (DHAA) to total AA], the levels of **thiobarbiturate reactive substance (TBARS)**, and the levels of lipid peroxides (LPO) in smokers, nonsmokers, and nonsmokers regularly exposed to environmental cigarette smoke (passive smokers). The study population consisted of 149 healthy males: 75 active smokers (consumption of > 15 cigarettes/day for more than 5 years), 36 passive smokers (more than 10 hr/week exposure to environmental cigarette smoke), and 38 nonsmokers (no cigarette smoke exposure). There were no significant differences in plasma **TBARS** and LPO levels among the three groups. Plasma levels of AA, the reduced form of vitamin C, were significantly lower in active smokers than in the combined non**smoking** groups (7.2 +/- 3.5 and 8.4 +/- 3.4 microg/mL, respectively; $p < 0.05$). Although no significant differences were found in plasma DHAA levels among the three groups, the ratios of DHAA to total AA were significantly higher in active and passive smokers than nonexposed nonsmokers (11.2, 10.3, and 7.1%, respectively; $p < 0.05$). These results indicate that passive **smoking**, as well as direct inhalation of cigarette smoke, affects the redox status of plasma AA. In passive smokers, the altered redox status of plasma AA suggests an oxidative stress.

PM3000457320

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

14: Diabet Med 1999 Nov;16(11):951-5

Impact of cigarette smoking on the incidence of Type 2 diabetes mellitus in middle-aged Japanese men: the Osaka Health Survey.

Uchimoto S, Tsumura K, Hayashi T, Suematsu C, Endo G, Fujii S, Okada K

Second Department of Internal Medicine, Osaka City University Medical School, Osaka, Japan.

AIMS: To assess the impact of cigarette **smoking** on the incidence of Type 2 diabetes mellitus (DM) in middle-aged Japanese men. METHODS: The study enrolled 6250 men aged 35-60 years and free of diabetes, impaired fasting glucose and hypertension at entry. Type 2 DM was defined by a fasting plasma glucose level > or =7.0 mmol/l or physician-diagnosed Type 2DM. RESULTS: Four hundred and fifty cases of Type 2 DM were confirmed during the 60904 person-years follow-up. After adjustment for multiple covariates, including age, body mass index, alcohol consumption, physical activity, parental history of diabetes and the level of fasting plasma glucose, total cholesterol, triglycerides, high-density lipoprotein cholesterol and haematocrit, the relative risk of Type 2 DM among current smokers compared with non-smokers was 1.47 (95% confidence interval (CI) 1.14-1.92). Men who smoked >30 cigarettes/day had a multivariate-relative risk of 1.73 (95% CI 1.20-2.48) compared with non-smokers. The number of cigarettes smoked daily and the pack-year values were positively related to the development of Type 2 DM in a dose-dependent manner (P for trends = 0.0026 and 0.001, respectively). CONCLUSIONS: A cigarette **smoking** habit is an independent risk factor for Type 2 DM.

15: Angiology 1999 Nov;50(11):959-61

Regarding "smoking is associated with dose-related increase of intima-media thickness and endothelial dysfunction".

Milionis HJ, Jeremy JY, Mikhailidis DP

Publication Types:
Comment
Letter

Comments:
Comment on: Angiology 1999 Mar;50(3):201-8

PM3000457321

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

16: Ann Biol Clin (Paris) 1999 Sep-Oct;57(5):573-8
[Effects of oral contraceptive preparations and smoking on lipoprotein repartition].
[Article in French]

Foulon T, Payen N, Groslambert P, Bijaoui S, Dupont G, Roland F, Laporte F
Laboratoire de biochimie A, CHU, BP 217, 38043 Grenoble Cedex 09.

We studied the effect of oral contraceptives and **smoking** on the lipid profile of 251 women and 72 men, 20-29-year-old. In women, taking estroprogestatives, cholesterol, triglycerides, apoproteins AI and B were higher than in controls; **HDL**-cholesterol was not modified. Lipoprotein analyses in polyacrylamide gradient gel exhibited an increase of the **HDL**3 fraction at the expense of the **HDL**2 fraction, with a reduced **LDL** size. **Smoking** in addition to estroprogestative absorption accentuated these modifications and led to a decreased **HDL**-cholesterol (**HDL**2 fraction essentially), with an increased **LDL**-cholesterol. In men, **smoking** resulted in higher levels of total cholesterol, apoprotein B and **LDL**-cholesterol, without any significant change in **LDL** size, higher levels of triglycerides and lower level of the **HDL**2 fraction without any change in **HDL**-cholesterol. In women, **smoking** led only to an increase in triglycerides. In summary, analysis of the distribution of **HDL** subclasses and of **LDL** size showed an evolution towards a supposed more atherogenic lipid profile in women taking oral contraceptives associated or not with **smoking**, and in male smokers.

17: Circulation 1999 Sep 14;100(11):1209-14
Alcohol consumption and stroke incidence in male smokers.

Leppala JM,Paunio M, Virtamo J,Fogelholm R, Albanes D, Taylor PR, Heinonen OP

Department of Public Health, University of Helsinki, Finland.

BACKGROUND: Studies on alcohol consumption and incidences of stroke subtypes have suggested distinct dose-response relationships. Blood pressure and **HDL** cholesterol mediate the effect of alcohol on coronary heart disease, but similar evidence on cerebrovascular diseases is not available. METHODS AND RESULTS: We studied the risk of stroke in 26 556 male cigarette smokers 50 to 69 years of age without history of stroke. The men were categorized as nondrinkers, light (</=24 g/d), moderate (25 to 60 g/d), or heavy (>60 g/d) drinkers. A total of 960 men suffered from incident stroke: 83 with subarachnoid and 95 with intracerebral hemorrhage, 733 with cerebral infarction, and 49 with unspecified stroke. The adjusted relative risk of subarachnoid hemorrhage was 1.0 in light drinkers, 1.3 in moderate drinkers, and 1.6 in heavy drinkers compared with nondrinkers. The respective relative risks of intracerebral hemorrhage were 0.8, 0.6, and 1.8; of cerebral infarction, 0.9, 1.2, and 1.5. Systolic blood pressure attenuated the effect of alcohol consumption in all subtypes of stroke, whereas **HDL** cholesterol strengthened the effect of alcohol in subarachnoid hemorrhage and cerebral infarction but attenuated the effect in intracerebral hemorrhage. CONCLUSIONS: Alcohol consumption may have a distinct dose-response relationship within each stroke subtype-linear in subarachnoid hemorrhage, U-shaped in intracerebral hemorrhage, and J-shaped in cerebral infarction-but further studies are warranted. Systolic blood pressure and **HDL** cholesterol seem to mediate the effect of alcohol on stroke incidence, but evidently additional mechanisms are involved.

PM3000457322

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

18: Respir Med 1999 Jun;93(6):389-96

Increased content of thiobarbituric acid-reactive substances and hydrogen peroxide in the expired breath condensate of patients with stable chronic obstructive pulmonary disease: no significant effect of cigarette smoking.

Nowak D, Kasielski M, Antczak A, Pietras T, Bialasiewicz P

Department of Pneumology and Allergology, Medical University of Lodz, Poland.

The imbalance between oxidants and antioxidants is known to play an important role in the pathogenesis of chronic obstructive pulmonary disease (COPD). Cigarette **smoking** is the most frequent factor responsible for development of COPD by leading to oxidant overload in the lower airways, due to presence of its own oxidants and to recruitment and activation of pulmonary phagocytes. We aimed to determine whether (1) patients with stable COPD have **higher thiobarbituric acid-reactive substances** (**TBARS**, an end-product of lipid peroxidation) and H2O2 levels in expired breath condensate than healthy subjects who have never smoked; (2) COPD subjects who are current smokers exhale more **TBARS** and H2O2 than COPD ex-smokers and those who have never smoked; and (3) concentration of **TBARS** correlates with H2O2 levels in the breath condensate of COPD patients. The TBAR and H2O2 content in expired breath condensate of 17 healthy non**smoking** subjects and 44 patients (11 current smokers, 20 ex-smokers and 13 who had never smoked) with stable COPD [forced expiratory volume in 1 s (FEV1) 63.3 +/- 16.3% and FEV1 reversibility 5.2 +/- 4.3% predicted value] was measured spectrofluorimetrically by the thiobarbituric acid and homovanillic acid methods, respectively. The mean concentrations of **TBARS** and H2O2 in the expired breath condensate of COPD subjects were 12 (0.48-0.86 microM vs. 0.04 +/- 0.14 microM; P < 0.05) and 10 times (0.48 +/- 0.67 microM vs. 0.05 +/- 0.07 microM; P < 0.005) higher than in healthy controls. Current smokers with COPD did not exhale more H2O2 than COPD ex-smokers and those who had never smoked. **TBARS** levels shared only a tendency to be higher in the breath condensate of **smoking** COPD subjects than in that of ex-smokers (0.92 +/- 1.49 microM vs. 0.35 +/- 0.44 microM) and of COPD subjects who had never smoked (0.92 +/- 1.49 microM vs. 0.30 +/- 0.53 microM). No correlation was found between TBAR and H2O2 levels in the whole COPD group. These variables did not correlate with cigarette **smoking** status and the time from **smoking** cessation. Subjects with stable COPD exhibit increased lipid peroxidation and H2O2 generation in the airways. Current cigarette **smoking** does not distinguish COPD subjects with respect to **TBARS** and H2O2 exhalation.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

19: Free Radic Biol Med 1999 Jul;27(1-2):60-8

Systemic and pulmonary oxidative stress in idiopathic pulmonary fibrosis.

Rahman I, Skwarska E, Henry M, Davis M, O'Connor CM, FitzGerald MX, Greening A, MacNee W

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An oxidant/antioxidant imbalance has been proposed in patients with idiopathic pulmonary fibrosis (IPF). We tested this hypothesis by measuring various parameters of the oxidant/antioxidant balance in the plasma of 12 patients with IPF (7 nonsmokers and 5 smokers); in the bronchoalveolar lavage fluid (BALF) of 24 patients with IPF (17 nonsmokers and 7 smokers) and 31 healthy subjects (23 nonsmokers and 8 smokers). The trolox equivalent antioxidant capacity (TEAC) in plasma and BALF was lower in non**smoking** patients with IPF (plasma 0.55+/-0.1 mM, p<.001; BALF 4.8+/-1.2 microM, mean +/-SEM, p<.01), compared with healthy nonsmokers (plasma 1.33+/-0.03 mM; BALF 10+/-2 microM). Similar trends in plasma and BALF TEAC were observed in **smoking** patients with IPF in comparison with healthy smokers. The decrease in BALF TEAC was concomitant with a decrease in BALF protein thiol levels, but the decrease TEAC levels in plasma in IPF patients was not accompanied by a decrease in protein thiol levels. Reduced glutathione (GSH) was lower in BALF in non**smoking** patients with IPF (1.0+/-0.1 microM) compared with healthy nonsmokers (2.3+/-0.2 microM, p<.001). In contrast, GSH levels were higher in **smoking** patients with IPF (5.2+/-1.1 microM, p<.001) than in non**smoking** patients. GSSG levels were not different in any of the groups. The levels of products of lipid peroxidation measured as **thiobarbituric acid reactive substances** (**TBARS**) in plasma and BALF were significantly increased in both **smoking** (plasma 2.2+/-0.5 microM, p<.01; BALF 0.18+/-0.04 microM, p<.001), and non**smoking** (plasma 2.1+/-0.3 microM, p<.01; BALF 0.22+/-0.05 microM, p<.001) IPF patients, compared with healthy nonsmokers (plasma 1.4+/-0.3 microM; BALF 0.05+/-0.004 microM). These data show evidence of oxidant/antioxidant imbalance in the lungs of patients with IPF, which is also reflected as systemic oxidant stress.

PM3000457324

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

20: Prostaglandins Other Lipid Mediat 1999 Jun;57(4):269-79

Maternal cigarette smoking increases F2-isoprostanes and reduces prostacyclin and nitric oxide in umbilical vessels.

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The objective of this study was to evaluate the influence of **smoking** on F2-isoprostanes, prostacylin and nitric oxide in human umbilical vessels. Umbilical cords from 13 babies of **smoking** mothers and from 28 babies of non-**smoking** mothers were examined for levels of F2-isoprostanes, prostacyclin, L-arginine, and L-citrulline. Forty-one umbilical arteries and eleven umbilical veins were analyzed. Statistical analysis of data was done using modified t-test. Cigarette **smoking** increased F2-isoprostane levels and reduced the generation of prostacyclin, L-arginine and L-citrulline comparably in umbilical arteries and veins. Notably, in umbilical cords of babies of non-**smoking** mothers the F2-isoprostane level was significantly higher in arteries. Cigarette **smoking** correlates with a direct vasoconstrictive effect. We suggest that **smoking** might enhance the vasoconstrictory capacity in umbilical arteries by increased F2-isoprostanes and by a simultaneous decrease in the production of the vasodilatory compounds, prostacyclin, and nitric oxide.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

21: J Am Coll Cardiol 1999 Jul;34(1):131-7

Hormone replacement therapy in postmenopausal women protects against smoking-induced changes in vascular structure and function.

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OBJECTIVES: The purpose of this study was to investigate the role of hormone replacement therapy (HRT) in postmenopausal women who smoke. BACKGROUND: Hormone replacement therapy appears to afford cardiovascular protection in postmenopausal women; however, in high risk individuals, specifically smokers, this has not been adequately studied. This question was addressed in a cross-sectional study of arterial structure, function and plasma lipids in postmenopausal smokers and nonsmokers. METHODS: Vascular ultrasound was performed in two age-matched groups of postmenopausal women, 70 on HRT (35 smokers) and 70 control subjects not on HRT (35 smokers). Indexes of arterial structure (carotid intima-media thickness [IMT]) and vascular function (systemic arterial compliance [SAC]) and lipid profiles were measured. RESULTS: Participant characteristics were similar in the two groups. Smokers on HRT, compared with **smoking** control subjects, had lower cholesterol (6.0+/-0.2 vs. 6.8+/-0.3 mmol/liter, p = 0.03) and more favorable mean values for IMT (0.64+/-0.02 vs. 0.74+/-0.03 mm, p = 0.007) and SAC (0.41+/-0.03 vs. 0.32+/-0.03 U/mm Hg, p = 0.03). Nonsmokers on HRT compared with non**smoking** control subjects had lower total cholesterol (5.7+/-0.2 vs. 6.5+/-0.2 mmol/liter, p = 0.02) and **low density lipoprotein** cholesterol (3.4+/-0.2 vs. 4.4+/-0.3 mmol/liter, p = 0.01). Mean IMT and SAC values in nonsmokers on HRT and control subjects were not significantly different. Multiple regression demonstrated significant correlation between HRT status and both IMT and SAC, in smokers and in those with increased cholesterol. In nonsmokers and those with lower cholesterol, HRT status was not significantly correlated with vascular parameters.
CONCLUSIONS:
In postmenopausal women who smoke there may be a beneficial effect of long-term estrogen therapy on indexes of arterial structure and function as surrogate markers of cardiovascular disease. Long-term controlled studies are needed to confirm these findings.

Comments:
Comment in: J Am Coll Cardiol 1999 Jul;34(1):138-9
Comment in: J Am Coll Cardiol 2000 Mar 1;35(3):815-6

PM3000457326

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

22: Eur J Appl Physiol Occup Physiol 1999 May;79(6):472-8

Effect of vitamin E supplementation on post-exercise plasma lipid peroxidation and blood antioxidant status in smokers: with special reference to haemoconcentration effect.

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The oxidative effects were investigated of exhausting exercise in smokers, and the possible protective role of 400 mg day(-1) vitamin E (Vit E) supplementation over a period of 28 days. The subjects exercised to exhaustion including concentric-eccentric contractions following maximal cycling. The haematocrit and haemoglobin, leucocyte (WBC), plasma lactic acid (La) and **malondialdehyde** (MDA), erythrocyte superoxide dismutase (SOD) and glutathione peroxidase (GPx), serum Vit E and ceruloplasmin (CER) concentrations were measured pre and post exercise. Supplementation increased Vit E concentrations 28% and 31% in the controls and the smokers, respectively. Cigarette **smoking** and/or Vit E supplementation did not influence plasma lipid peroxidation or the antioxidant status at rest. Exercise caused significant haemoconcentration in all groups. When the post-exercise concentrations were adjusted for haemoconcentration, a significant elevation in La concentrations due to exercise was observed in all groups. Similarly, there were significant elevations in the adjusted WBC counts in all groups except the Vit E supplemented controls. The **MDA** concentrations on the other hand, when adjusted for haemoconcentration, did not exhibit any difference due to exercise. Exercise did not affect the GPx and CER activities either, while causing a SOD activity loss in all groups except the Vit E supplemented non-smokers. Serum Vit E concentrations diminished significantly in all groups after exercise. Post-exercise plasma **MDA** and blood antioxidant concentrations were not altered by **smoking**. The results would suggest that plasma volume changes should always be taken into account when assessing post-exercise plasma concentrations and that **smoking** and exercise do not have an additional collective effect on plasma lipid peroxidation and the dose of Vit E administered was insufficient to maintain the serum concentrations after exercise.

Publication Types:
Clinical trial
Randomized controlled trial

PM3000457327

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

23: Contraception 1999 Jan;59(1):17-23

Effect of oral contraceptives containing 20 and 35 micrograms ethinyl estradiol on urinary prostacyclin and thromboxane metabolite levels in smokers and nonsmokers.

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The interaction between **smoking** and oral contraceptive (OC) use with respect to thrombogenesis was investigated by studying the effects of OC and **smoking** on urinary prostacyclin (PGI2) and thromboxane A2 (TxA2) metabolite levels in smokers and nonsmokers. Sixty healthy women, aged 19-32 years, who were not taking any hormonal treatment for at least 3 months before initiating the study, were divided into three equal groups: OC users who smoked (N = 20), OC users who did not smoke (N = 20), and a control group of 10 smokers and 10 nonsmokers. Each OC treatment group was randomized to receive either norethindrone (NET) acetate (1 mg)/ethinyl estradiol (EE2) (35 micrograms) (N = 10) or NET acetate (1 mg)/EE2 (20 micrograms) (N = 10) daily for 3 months. Overnight urine collections and fasting blood samples were obtained at baseline and at the end of the 3-month study. Serum levels of NET and EE2, as well as urinary levels of cotinine and the stable metabolites of PGI2 and TxA2, namely 6-keto-prostaglandin F1 alpha (6-keto-PGF1 alpha) and **thromboxane (TxB2)**, respectively, were measured by specific immunoassays. Analysis of pre- to posttreatment changes in mean urinary 6-keto-PGF1 alpha and **TxB2** levels for each subgroup, as determined by **smoking** status and EE2 dose, showed no statistically significant differences. Also, no significant differences were found in each subgroup with respect to changes in the 6-keto-PGF1 alpha/**TxB2** ratios. Large intersubject variability in urinary 6-keto-PGF1 alpha and **TxB2** levels were observed in all subgroups. The results of this study indicate that both low-estrogen-dose compounds, when used by smokers or nonsmokers, did not significantly alter the ratio of PGI2 to TXA2 metabolites, compared with pretreatment. However, the small number of subjects and the large intersubject variability in this study make it difficult to determine if there is a significant difference between the 20- and 30-microgram EE2 doses.

Publication Types:
Clinical trial
Randomized controlled trial

PM3000457328

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

24: Can J Cardiol 1999 Apr;15(4):428-33

Prevalence of high plasma triglyceride combined with low HDL-C levels and its association with smoking, hypertension, obesity, diabetes, sedentariness and LDL-C levels in the Canadian population.

Canadian Heart Health Surveys Research Group.

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OBJECTIVE: To report the associations of plasma triglyceride, **high density lipoprotein cholesterol (HDL-C)** and **low density lipoprotein cholesterol (LDL-C)** with nonlipid coronary artery disease risk factors. In particular, the associations for persons with high triglyceride and low **HDL-C** levels were examined. DESIGN: A stratified random probability sample of 29,855 men and women aged 18 to 74 years from the Canadian Heart Health Surveys (1986 to 1992) in 10 provinces. Blood samples were obtained from 18,555 participants who had fasted for 8 h or more. Plasma lipids were determined at the J Alick Little Lipid Research Laboratory, Toronto, Ontario, with standardization of the Centers for Disease Control Lipid Standardization Program, Atlanta. OUTCOME MEASURES: Fasting plasma total cholesterol, triglyceride, **LDL-C** and **HDL-C** levels. MAIN RESULTS: The prevalence of men with triglyceride levels above 1.7 mmol/L and **HDL**-C levels below 0.9 mmol/L was 10%, compared with 3% for men with triglyceride levels below 1.7 mmol/L and **HDL-C** levels below 0.9 mmol/L. The prevalence of women with triglyceride levels above 1.7 mmol/L and **HDL-C** levels below 0.9 mmol/L was 3% compared with a prevalence of less than 1% for women with triglyceride levels below 1.7 mmol/L and **HDL-C** levels below 0.9 mmol/L. Even when plasma **LDL-C** was low at less than 3.4 mmol/L, there was an age trend for increasing prevalences of the combination of triglyceride levels 2.3 mmol/L or greater and **HDL**-C levels less than 0.9 mmol/L in both sexes. The prevalence of a triglyceride levels 2.3 mmol/L or greater combined with an **HDL**-C level below 0.9 mmol/L was increased in groups who were cigarette smokers, diabetic, hypertensive, obese or sedentary, or who had higher **LDL-C** levels in both sexes, and the increase was even greater in the presence of two or more of these other risk factors. CONCLUSIONS: Among men or women with low **HDL**-C and high triglyceride levels, **smoking**, diabetes, sedentariness, hypertension and obesity were much more prevalent than among those at low risk with high **HDL**-C and low triglyceride levels.

25: Clin Chem 1999 Apr;45(4):577-8

Measurement of protein carbonyls in plasma of smokers and in oxidized LDL by an ELISA.

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Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

26: J Toxicol Environ Health 1999 Mar 26;56(6):373-8

Effects of smoking on plasma and erythrocyte antioxidant defense systems.

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In this study, activities of superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), and catalase (CAT) enzymes were measured in the erythrocytes, and levels of **thiobarbituric acid-reactive substances** (**TBARS**) and antioxidant potential (AOP) values were measured in both erythrocyte and plasma samples from smokerS and nonsmokers. No significant differences were observed in erythrocyte parameters, serum triglycerides, and total cholesterol. AOP was significantly lower and **TBARS** level higher in the plasma samples from smokers compared with those of nonsmokers. Results suggest that **smoking** causes no impairment in the enzymatic antioxidant defense system and does not lead to oxidant stress in the erythrocytes, possibly because these cells have potent antioxidant defense capacity.

PM3000457330

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

27: Angiology 1999 Mar;50(3):201-8

Smoking is associated with dose-related increase of intima-media thickness and endothelial dysfunction.

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Cigarette **smoking** is firmly established as a risk factor for atherosclerosis. However, the exact mechanism causing **smoking**-related damage to the arterial wall and its relation to the atherosclerotic process is not known. Also unknown is the time delay between the start of **smoking** and the sequence of functional and morphologic changes occurring in the arterial wall caused by **smoking** and their interrelationship. Therefore, the aim of this study was to evaluate the acute and chronic effects of **smoking** on endothelium-dependent (flow-mediated) dilation (FMD) of the peripheral arteries, the effects of dose and duration of chronic **smoking** on intima-media thickness (IMT) of the carotid arteries, and their interrelationship. The study encompassed two groups of smokers. In group A there were 40 subjects of both sexes, who smoked on average 17.6 +/- 6.5 cigarettes per day, for 5 to 15 years (mean 8.95 +/- 4.0 years), mean age 28.1 years. Group B consisted of 42 smokers of both sexes who smoked 21.15 +/- 8.2 cigarettes/day for more than 15 years (mean 21.15 +/- 3.4 years), mean age 39.5 years. The control group consisted of 40 healthy subjects without major risk factors of atherosclerosis, mean age 29.1 years. By means of high-resolution ultrasound the brachial artery diameter was measured at rest and during reactive hyperemia (after release of a forearm tourniquet) and the flow-mediated, endothelium-dependent dilation was calculated. The IMT of the carotid arteries was determined in all subjects by use of B-mode ultrasonography. Resting blood flow in the brachial arteries was significantly less in the smokers' groups than in controls (78.8 +/- 31.9 vs 134.9 +/- 45.0 mL/min, p<0.0001). This decrease was much more evident in female than in male smokers. Female smokers also had significantly smaller brachial artery diameter at rest. In smokers the FMD of the brachial artery was reduced (11 +/- 4% vs 7 +/- 4%, p<0.004) and the mean IMT was significantly greater than in controls (0.68 +/- 0.13 vs 0.59 +/- 0.04 mm, p<0.001). Impairments of FMD and IMT increase were related to the duration and to the number of cigarettes smoked. In all subjects IMT was significantly correlated with total and **LDL** cholesterol, **fibrinogen**, lipoprotein(a) concentration, body mass index, and age of the subjects, but multivariate analysis showed that only total dose smoked and **fibrinogen** concentration were independently related to IMT. The results of this study show that **smoking** is associated with dose-related impairment of FMD and increased IMT of the carotid arteries. Impairment of FMD occurs in smokers very early and is the earliest detectable event, preceding morphologic changes of the vessel wall. Some harmful effects of **smoking** on the vessel wall are gender related.

Comments:
Comment in: Angiology 1999 Nov;50(11):959-61

PM3000457331

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

28: J R Soc Health 1998 Apr;118(2):91-3
Smoking, diabetes and hyperlipidaemia.

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The epidemiological evidence linking **smoking** with insulin resistance is considerable. This evidence is even more convincing because there is a dose response relationship between **smoking** and the risk of non-insulin dependent diabetes (NIDDM). Similarly, there is a time-dependent decrease in risk of NIDDM for those who quit **smoking**. Insulin resistance (in the form of impaired glucose tolerance, IGT) may precede the development of NIDDM. There is a biochemical basis for the **smoking**-IGT/NIDDM relationship. **Smoking** increases the risk of developing diabetic complications like nephropathy, neuropathy and retinopathy **Smoking** is also an independent risk factor for myocardial infraction and all-cause mortality in NIDDM. Smokers are both insulin resistant and lipid intolerant. **Smoking** cessation increases circulating high density lipoprotein (**HDL**) and reduces low density lipoprotein (**LDL**) levels, despite weight gain. Those providing advice or treatment to improve cardiovascular risk factors should be aware of these **smoking**-related harmful effects. This is especially true if IGT is underdiagnosed despite the fact that this condition increases the risk of vascular events. Explaining that **smoking** increases the chance of developing diabetes as well as raising 'blood fat' levels may convince more smokers to quit.
Review, tutorial

29: Int J Vitam Nutr Res 1999 Jan;69(1):45-51
Oxidative stress in smokers supplemented with vitamin C.

Aghdassi E, Royall D, Allard JP
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The ability of vitamin C supplement to influence lipid peroxidation and pulmonary function tests in healthy smokers was investigated. In this randomized double blind controlled trail, 56 smokers (S) received either 500 mg of vitamin C (C) or placebo (P) daily for 4 weeks. All completed the trial. Both groups were comparable and the number of cigarettes smoked were C: 14.2 +/- 1.8 and P: 18.3 +/- 2.0 pack-years. Plasma vitamin C concentrations increased significantly ($p < 0.005$) only in the group supplemented with vitamin C. Lipid peroxidation measured by breath pentane output (BPO) (C: 7.5 +/- 1.4 vs P: 7.0 +/- 1.3 pmol.kg-1.min-1) and plasma HPLC-separated **malondialdehyde** (MDA) (C: 0.58 +/- 0.05 vs P: 0.47 +/- 0.05 nmol.ml-1) were not significantly different between the 2 groups at baseline and did not change after four weeks of vitamin C supplementation (BPO: C: 5.3 +/- 0.9 vs P: 5.5 +/- 0.9 pmol.kg-1.min-1; HPLC-MDA: C: 0.50 +/- 0.07 vs P: 0.42 +/- 0.07 nmol.ml-1). No changes were detected in pulmonary function tests even in heavy smokers. Therefore, 4 week supplementation with 500 mg of vitamin C did not change lipid peroxidation indices and had no effect on pulmonary function tests.
Clinical trial
Randomized controlled trial

PM3000457332

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

30: Arch Biochem Biophys 1999 Feb 15;362(2):309-16

Concurrent increase of oxidative DNA damage and lipid peroxidation together with mitochondrial DNA mutation in human lung tissues during aging--smoking enhances oxidative stress on the aged tissues.

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Although mutation of mitochondrial DNA (mtDNA) in human tissues has been established to associate with intrinsic aging, the impact of environmental factors on the formation and accumulation of mtDNA mutations and oxidative DNA damage in human tissues is poorly understood. We have investigated the levels of mtDNA with the 4977-bp deletion and A3243G point mutation, oxidative DNA damage (indicated by the formation of 8-hydroxy-2'-deoxyguanosine, 8-OH-dG), and lipid peroxides in lung tissues from smokers and nonsmokers of subjects of different ages. The results showed concurrent age-dependent increase of the 4977-bp deleted mtDNA ($P < 0.001$), 8-OH-dG ($P < 0.05$), and lipid peroxides ($P < 0.05$) in the human lung. In the group of subjects above 60 years old, smokers had more extensive DNA damage and lipid peroxidation than did the nonsmokers. However, the levels of mtDNA with the 4977-bp deletion and A3243G point mutation in the lung of smokers were not significantly different from those of the age-matched nonsmokers. Taken together, these results suggest that accumulation of mtDNA with the 4977-bp deletion together with oxidative DNA damage and lipid peroxides is associated with aging and that **smoking** enhances oxidative damage in human lung tissues.
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PM3000457333

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

31: Am J Obstet Gynecol 1999 Feb;180(2 Pt 1):476-82

Stem villous arteries from the placentas of heavy smokers: functional and mechanical properties.

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OBJECTIVE: The aim of the study was to compare the mechanical and functional properties of isolated small stem villous arteries from the placentas of women who smoked heavily (>/=15 cigarettes/d) during pregnancy with those from the placentas of nonsmokers. STUDY DESIGN: Isolated stem villous arteries were mounted in small-vessel myographs. Circumference-tension relationships were established with 124 mmol/L potassium chloride. Concentration-response curves were obtained for endothelin 1, prostaglandin F2alpha, vasoactive intestinal peptide, corticotropin-releasing hormone, sodium nitroprusside, and cadmium chloride. The effect of nitric oxide was examined with N omega-nitro-l -arginine. RESULTS: Stem villous arteries from the heavy **smoking** group developed a significantly lower tension than did those from nonsmokers at 6 of 9 steps of the circumference-tension experiment (P <.05). Endothelin 1 evoked a significantly greater maximum vasoconstrictive response in stem villous arteries from heavy smokers than in those from nonsmokers (P <.05). CONCLUSION: Stem villous arteries of heavy smokers have altered mechanical properties and a greater vasoconstrictive response to endothelin 1 than do those from nonsmokers. These changes may compromise fetal placental blood flow and thereby contribute to the lower birth weights seen among infants born to heavy smokers.

PM3000457334

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

32: J Am Coll Cardiol 1999 Feb;33(2):499-505

Effect of vitamin E on endothelial vasodilator function in patients with hypercholesterolemia, chronic smoking or both.

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OBJECTIVES: The purpose of this study was to test the hypothesis that long-term supplementation with Vitamin E improves endothelium-dependent relaxation in hypercholesterolemia patients and/or chronic **smoking**, two risk factors that have been shown to be associated with increased radical formation. BACKGROUND: Experimental evidence suggests that oxidized low density lipoprotein (**LDL**) impairs endothelium-dependent relaxation, and vitamin E, a lipid-soluble antioxidant, reduces the oxidation of **LDL**. METHODS: Thirteen subjects with hypercholesterolemia, 14 smokers and 15 hypercholesterolemic smokers were enrolled in a double-blind, placebo-controlled study. After baseline measurements of plasma autoantibodies against oxidized **LDL** and assessment of endothelium-dependent relaxation using intra-arterial forearm infusions of acetylcholine, participants within each group were randomly assigned in a 1:2 fashion to receive either placebo or vitamin E for 4 months, when plasma levels of autoantibodies against oxidized **LDL** and vascular function were reassessed. RESULTS: Vitamin E significantly augmented endothelium-dependent relaxation in hypercholesterolemic smokers but not in patients with either hypercholesterolemia or chronic **smoking**. At baseline, hypercholesterolemic smokers had significantly higher autoantibody levels against oxidized **LDL** (compared with the other two groups), which were significantly reduced after 4 months of vitamin E supplementation. There was a significant relationship between improvement in acetylcholine-induced vasodilation and the change in autoantibody titer against oxidized **LDL** ($r = -0.59$; $p = 0.002$). CONCLUSIONS: Long-term vitamin E supplementation improves endothelium-dependent relaxation in forearm resistance vessels of hypercholesterolemic smokers, which are characterized by increased levels of autoantibodies against oxidized **LDL**. These findings may suggest that the beneficial effect of vitamin E is confined to subjects with increased exposure to oxidized **LDL**.

Publication Types:
Clinical trial
Randomized controlled trial

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

33: Environ Res 1999 Jan;80(1):18-24

Age-associated alteration of blood thiol-group-related antioxidants in smokers.

Liu CS, Wei YH
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Total blood glutathione and nonglutathione free sulfhydryl compounds, glutathione peroxidase, and glutathione S-transferase in erythrocytes and plasma and also lipid peroxides in plasma were investigated in 48 male smokers and 42 male nonsmokers. We found that the level of total blood glutathione was significantly increased in young smokers (age <40) but no such change was noted in aging smokers (age>/=40). The activities of glutathione peroxidase and glutathione S-transferase in plasma were significantly decreased in young smokers and the plasma levels of these two enzymes and nonglutathione free sulfhydryl compounds were more drastically decreased in aging smokers. The average concentration of plasma lipid peroxides of the aging smokers (2.76+/-0.46 nmol/ml) was significantly higher than that of the aging nonsmokers (2.32+/-0. 41nmol/ml, P=0.049). On the other hand, the level of total blood glutathione was negatively correlated with the level of plasma lipid peroxides (r=-0.305, P=0.002) and was positively correlated with the **smoking** index (r=0.307, P=0.019) of all the study subjects under age control. These results indicate that the activities of glutathione peroxidase and glutathione S-transferase declined to a great extent under **smoking**-mediated oxidative stress in the blood of both young and aging smokers. Moreover, the compensatory generation of total blood glutathione may effectively prevent plasma lipids from peroxidation in young smokers, although the activities of glutathione peroxidase and glutathione S-transferase in plasma were decreased. By contrast, total blood glutathione was inadequate for such protection in the aging smokers. We suggest that supplementation of thiol-group-related agents may be considered for the prevention or alleviation of oxidative stress in aging smokers, whose capability and capacity for the disposal of **smoking**-mediated free radicals and reactive oxygen species are compromised. Copyright 1999 Academic Press.

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Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

34: Am J Respir Crit Care Med 1999 Feb;159(2):473-9
Epithelial permeability, inflammation, and oxidant stress in the air spaces of smokers.

Morrison D, Rahman I, Lannan S, MacNee W
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The mechanism responsible for the increased air-space permeability in cigarette smokers is unknown. The aim of this study was to assess the acute and chronic effects of cigarette **smoking** on epithelial permeability, inflammation, and oxidant stress in the air spaces of smokers. Fourteen cigarette smokers underwent 99mTc-diethylenetriamine pentaacetic acid (99mTc-DTPA) lung scans after abstaining from **smoking** for 12 h (chronic **smoking**) and 1 h after **smoking** two cigarettes (acute **smoking**). Each smoker also underwent bronchoscopy and bronchoalveolar lavage (BAL) after either chronic (n = 8) or acute **smoking** (n = 7). Seven nonsmokers also underwent bronchoscopy and BAL. The time to 50% clearance of 99mTc-DTPA (t50) after chronic **smoking** was 16.7 +/- 1. 3 min (mean +/- SE), and was further reduced after acute **smoking** to 14.8 +/- 1.0 min ($p < 0.01$). Neutrophil numbers were increased in bronchoalveolar lavage fluid (BALF) in the acute **smoking** group as compared with the nonsmokers ($p < 0.05$). Superoxide release from mixed BAL leukocytes was increased after chronic ($p < 0.01$) and acute ($p < 0.001$) **smoking**, as were thiobarbituric acid-reactive species (**TBARS**), providing evidence of lipid peroxidation in plasma (chronic, $p < 0.05$; acute, $p < 0.05$). Trolox equivalent antioxidant capacity (TEAC) was reduced in plasma ($p < 0.001$) and increased in BALF ($p < 0.05$) in both **smoking** groups. The study therefore showed an acute increase in epithelial permeability and an increase in the number of neutrophils in the air spaces of cigarette smokers concomitant with evidence of increased oxidant stress.

35: Hunan I Ko Ta Hsueh Hsueh Pao 1997;22(2):149-52
[Effects of smoking on oxygen free radicals and fibrinolytic system].

[Article in Chinese]

Wang Q, Zhou H, Sun M, Jia Z

Department of Cardiac Medicine, Xiangya Hospital, Hunan Medical University, Changsha.

The effects of **smoking** on SOD, MDA, t-PA, PAI-1 were studied in 20 healthy men (10 smokers and 10 nonsmokers). RESULTS: SOD decreased and MDA increased significantly in smokers. After acute **smoking**, SOD decreased and MDA increased significantly in all the subjects, t-PA and PAI-1 activities were increased immediately after acute **smoking**. There was a significant positive relationship between increased t-PA and SOD, whereas a significant negative relationship exists between increased t-PA and MDA. CONCLUSION: **Smoking** increases oxygen free radicals. The release of t-PA is decreased in smokers, that might be resulted from the increases of oxygen free radicals.

PM3000457337

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

36: Eur J Gastroenterol Hepatol 1998 Jul;10(7):573-8

Plasma free radical activity and antioxidant vitamin levels in dyspeptic patients: correlation with smoking and Helicobacter pylori infection.

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BACKGROUND: The pathological processes by which Helicobacter pylori infection leads to the development of gastroduodenal disease are still incompletely understood. Oxygen-derived free radicals are important mediators of inflammation and potential carcinogens. Furthermore, dietary studies have suggested that antioxidant vitamins may protect against gastric cancer. OBJECTIVE: To determine plasma free radical activity and antioxidant vitamin levels in dyspeptic patients and to correlate the results with H. pylori infection and tobacco **smoking**. SUBJECTS: Forty-three patients undergoing routine endoscopy for investigation of dyspepsia. METHODS: Plasma free radical activity was determined by measurement of **thiobarbituric acid-reactive substances** (**TBARS**). Plasma samples were also assayed for the antioxidant vitamins A, C and E. Gastroduodenal biopsies were obtained from all patients for histological examination. RESULTS: Plasma **TBARS** levels were significantly higher in H. pylori positive versus negative subjects ($P < 0.03$), smokers versus non-smokers ($P < 0.04$) and males versus females ($P < 0.01$). Multiple regression analysis revealed that after correcting for male sex and **smoking** there was no significant association between plasma free radical activity and H. pylori infection. Smokers had significantly lower levels of plasma vitamin C than non-smokers ($P< 0.05$); no differences were seen in vitamin A and E levels. Gender and H. pylori infection did not significantly affect plasma antioxidant vitamin levels. Gastroduodenal disease was present in all of the smokers compared with 67% of the non-smokers ($P < 0.05$); 69% of the smokers were H. pylori positive versus 53% of the non-smokers. CONCLUSIONS: Tobacco **smoking** and male sex, both recognized risk factors for gastroduodenal disease, appear to be the major determinants of increased plasma free radical activity in dyspeptic subjects, rather than H. pylori infection. The reason for the higher prevalence of H. pylori infection and gastroduodenal disease in dyspeptic smokers is unclear but may relate to weakened antioxidant defences.

PM3000457338

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

37: Am J Respir Cell Mol Biol 1998 Dec;19(6):901-9

Smoking-associated mitochondrial DNA mutations and lipid peroxidation in human lung tissues.

Fahn HJ, Wang LS, Kao SH, Chang SC, Huang MH, Wei YH

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To investigate the effect of cigarette **smoking** on mitochondrial DNA (mtDNA) mutation and lipid peroxidation in lung tissues, 152 samples from lung resections were collected. A novel deletion of 4,839 bp of mtDNA was found in 80 (52.6%) of the 152 lung samples. The breakpoints of the 4,839-bp mtDNA deletion were flanked by a nine-nucleotide direct repeat (5'-CATACACAA-3'). The frequency of occurrence and the proportion of the 4,839-bp mtDNA deletion in the lung increased significantly with the **smoking** index in terms of pack-years ($P < 0.05$). The incidence and proportion of the 4,839-bp mtDNA deletion in the lung tissues of current smokers were significantly higher than in those of nonsmokers ($P < 0.05$). In addition, we found that the content of lipid peroxides in the lung tissues of the smokers was significantly higher than in that of nonsmokers, and increased with the **smoking** index. The average **malondialdehyde** level in the lung tissues was 12.81 +/- 4.99 micromol/g for subjects with a **smoking** index of more than 50 pack-yr, and was 5.39 +/- 0.48 micromol/g for nonsmokers ($P < 0.05$). Multiple regression analysis showed that the **smoking** index, tissue lipid-peroxide content, and FEV1/FVC ratio were correlated with the proportion of the 4,839-bp mtDNA deletion in the lung. These results suggest that cigarette smoke plays an important role in the increase in mtDNA mutation and lipid peroxidation in the lung tissues of smokers.

PM3000457339

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

38: Arch Mal Coeur Vaiss 1998 Oct;91 Spec No 5:59-63

[Heart and brain: are the risk factors the same? Are the results of primary and secondary trials comparable]?

[Article in French]

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The aim of this study was to identify the similitudes and the differences in the epidemiology and prevention of myocardial infarction and cerebrovascular accidents by analysis of trials of primary and secondary prevention of myocardial infarction and cerebrovascular accidents. The principal risk factors common to both pathologies are hypertension, **smoking** and increased **LDL**-cholesterol. However, the statistical significance with respect to causality differs from one pathology to the other. Similarly, the impact of preventive measures is not the same: the treatment of hypertension is more important in the prevention of cerebrovascular accidents than myocardial infarction; the situation is the other way around with respect to the treatment of hypercholesterolaemia. Of the therapeutic interventions, aspirin is effective in all stages of coronary artery disease but does not prevent cerebrovascular accidents in patients without documented atherosclerosis. Thrombolysis carries a much higher benefit/risk ratio in the treatment of myocardial infarction than in that of cerebral infarction. The so-called cardioprotective drugs, such as the betablockers and angiotensin converting enzyme inhibitors, have only been used to any extent in the secondary prevention of myocardial infarction. These differences reflect the fact that cerebrovascular accident covers a range of diseases much more diverse than does myocardial infarction, and also that the brain is much more exposed to haemorrhage whereas cardiac haematoma is highly unusual. Finally, cerebral atherosclerosis is a later event than coronary atherosclerosis and this has epidemiological implications which are difficult to assess. In conclusion, the prevention of myocardial infarction and of cerebrovascular accidents may proceed theoretically by a common pathway but in practice, it is very different.

PM3000457340

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

39: Eur J Epidemiol 1998 Sep;14(6):525-33

Life-style factors associated with changes in serum lipids in a follow-up study of cardiovascular risk factors.

Martinez-Gonzalez MA, Fernandez-Garcia J, Sanchez-Izquierdo F, Lardelli-Claret P, Jimenez Moleon J, Galvez-Vargas R

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We studied some life-style characteristics that may predict changes in total serum cholesterol and cholesterol bound to high density lipoproteins (**HDL**-cholesterol) in a sample of 980 healthy Spanish employees of both sexes who were followed for three years. All workers participated in a multifactorial program aimed at preventing cardiovascular disease. Linear regression models were fitted with changes in total and **HDL**-cholesterol as the dependent variables, after eliminating variability due to the influence of basal values. The association between lifestyle factors and lipid changes was controlled for dietary modifications. In the multivariate analysis, decreases in body mass index, and in alcohol consumption were associated with significant reductions in total serum cholesterol. Maintaining sports at post-test or starting to practice them in the interim was also significantly and independently associated with favourable changes in serum cholesterol. Leisure-time exercise ($p = 0.002$) and giving up **smoking** ($p = 0.06$) were each associated with increased **HDL**-cholesterol.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

40: Eur J Clin Invest 1998 Jul;28(7):584-91

The effect of smoking on post-heparin lipoprotein and hepatic lipase, cholesteryl ester transfer protein and lecithin:cholesterol acyl transferase activities in human plasma.

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INTRODUCTION: **Smoking** is associated with dyslipidaemia, particularly raised plasma triglycerides and reduced high-density lipoprotein (**HDL**)-cholesterol and a delayed clearance of triglyceride in fat tolerance tests. The aim of this study was to investigate whether these phenomena could be explained by a reduced lipoprotein lipase activity in smokers. METHODS: A group of 40 healthy individuals [plasma cholesterol 5.07 (SD 0.90) mmol L-1, plasma triglyceride 1.02 (SD 0.39) mmol L-1)] was studied to examine the effects of **smoking** on plasma enzyme activities, particularly post-heparin lipase activities. The group comprised 20 smokers and 20 non-smokers, who were matched for age, gender and body mass index (BMI). RESULTS: Post-heparin lipoprotein lipase (LPL) activity [3.89 (SD 1.58) vs. 5.85 (SD 2.30) mumol free fatty acids (FFA) mL-1 h-1, P < 0.005], but not post-heparin hepatic lipase (HL) activity, was reduced in smokers. Plasma cholesteryl ester transfer protein (CETP) activity and lecithin: cholesterol acyl transferase (LCAT) activity were measured in a subgroup of 18 individuals, comprising nine smokers with nine matched non-smokers. There was no difference in CETP activities between two groups, but smokers had a significantly reduced plasma LCAT activity [112 (SD 23) vs. 152 (SD 24) nmol cholesterol mL-1 h-1, P < 0.005]. In both smokers (r=-0.53, P < 0.05) and non-smokers (r=-0.54, P < 0.05), **HDL**2 concentration was negatively associated with HL activity. In non-smokers, **HDL**3 concentration was negatively associated with CETP activity (r= -0.77, P < 0.05), whereas in smokers **HDL**3 concentration was negatively associated with LCAT activity (r= -0.78, P < 0.050). CONCLUSION: It was shown by direct measurement that the activity of plasma post-heparin LPL is reduced in smokers, independently of age, gender and BMI. It is concluded that this enzyme perturbation associated with **smoking** may contribute to the development of the atherogenic lipoprotein phenotype seen in smokers.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

41: Am J Clin Nutr 1998 Aug;68(2):319-27
Published erratum appears in Am J Clin Nutr 1999 Jun;69(6):1293
Antioxidant vitamin supplementation and lipid peroxidation in smokers.

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Previous studies have shown that cigarette smoke enhances lipid peroxidation. This study examined the effect of daily consumption of a tomato-based juice supplemented with vitamin C (600 mg), vitamin E (400 IU, or 400 mg), and beta-carotene (30 mg) on various indexes of lipid peroxidation (breath pentane excretion and susceptibility of **LDL** to copper-mediated oxidation) in smokers. In addition, plasma lycopene and vitamin concentrations and total peroxyl radical trapping potential, a measure of antioxidant defenses, were assessed. Relative to the placebo juice, the vitamin-supplemented juice resulted in a significant decrease in breath-pentane excretion as well as a significant improvement in the resistance of **LDL** to oxidation. The lag phase of conjugated diene formation lengthened and the propagation rate decreased, indicating a decreased susceptibility of **LDL** to oxidative modification. Increased concentrations of plasma vitamin C, beta-carotene, and lycopene were found to be significantly correlated with the conjugated diene lag phase and rate of formation. Vitamin E was highly correlated with beta-carotene. Plasma total peroxyl radical trapping potential values did not change in response to supplementation. This study thus indicates that an antioxidant-supplemented drink can reduce lipid peroxidation and susceptibility of **LDL** to oxidation in smokers and may ameliorate the oxidative stress of cigarette smoke.
Publication Types:
Clinical trial
Controlled clinical trial

Comments:
Comment in: Am J Clin Nutr 1999 Jun;69(6):1292

PM3000457343

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

42: J Intern Med 1998 Jul;244(1):33-41

Associations of smoking, alcohol and physical activity with risk factors for coronary heart disease and diabetes in the first follow-up cohort of the Heart Disease and Diabetes Risk Indicators in a Screened Cohort study (HDDRISC-1).

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OBJECTIVES: To investigate the associations between risk factors for cardiovascular disease and cigarette **smoking**, alcohol intake, and physical activity in a group of predominantly healthy men. DESIGN: Cohort study with baseline characterisation, clinical follow-up, and identification of predictors of coronary artery disease and diabetes. SETTING: University hospital metabolic day ward. SUBJECTS: Participants in a company health programme (n=742). MAIN OUTCOME MEASURES: Routine haematology and biochemistry, cholesterol, triglycerides, high density lipoprotein (**HDL**) cholesterol (on a subset of 522 subjects), and glucose and insulin levels during a 3 h oral glucose tolerance test (OGTT). RESULTS: Independent associations with previous cigarette **smoking** included high uric acid and low **HDL** cholesterol, and with current cigarette **smoking**, high haemoglobin and white cell count and low OGTT insulin. Increasing alcohol intake was associated with increasing blood pressure, uric acid, **HDL** cholesterol and fasting glucose. The moderate range of exercise intensity in this cohort was associated with decreasing systolic blood pressure, fasting insulin and OGTT glucose and insulin. Factor analysis distinguished principal factors comprising features of the metabolic syndrome with low physical activity, and high white cell count, high haemoglobin concentration and low **HDL** cholesterol with increasing previous and current cigarette **smoking** and alcohol intake. CONCLUSIONS: Some characteristics of the metabolic syndrome were seen with previous but not current **smoking** habit. Regular alcohol consumption was associated with mainly unfavourable metabolic characteristics, although there was an independent beneficial association with **HDL** cholesterol. The improved metabolic syndrome profile seen with increasing exercise is consistent with even moderate degrees of physical activity having beneficial effects on metabolism.

PM3000457344

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

43: J Lipid Res 1998 Jul;39(7):1493-502

Decreased postprandial high density lipoprotein cholesterol and apolipoproteins A-I and E in normolipidemic smoking men: relations with lipid transfer proteins and LCAT activities.

Mero N, Van Tol A, Scheek LM, Van Gent T, Labeur C, Rosseneu M, Taskinen MR

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We have previously reported that normolipidemic smokers are lipid intolerant due to incr eased responses of triglyceride-rich lipoproteins (TRL) apolipoprotein B-48, triglyceride (TG), and retinyl esters to a mixed meal compared to non-smokers. To investigate whether postprandial high density lipoprotein (**HDL**), apolipoprotein A-I (apoA-I), apolipoprotein A-II (apoA-II), and apolipoprotein E (apoE) concentrations or lipid transfer protein activities are affected by cigarette **smoking**, we investigated 12 male smokers and 12 non-smokers with comparable fasting lipoprotein profile, BMI, and age. Plasma samples obtained after an overnight fast and postprandially were separated by density gradient ultracentrifugation. Postprandial apoA-I, lipoprotein AI-particles (LpA-I), **HDL**-cholesterol, and **HDL** apoE concentrations decreased in smokers, but remained unchanged in controls. Concomitantly, cholesterol and apoE concentrations increased significantly in TRL fractions in smokers. Fasting lecithin:cholesterol acyltransferase (LCAT) and phospholipid transfer protein (PLTP) activity levels, as well as esterification rates (EST) and phospholipid transfer rates were comparable between the groups. Cholesteryl ester transfer protein (CETP) activity levels were lower in the smokers. Postprandially EST increased, but CETP and PLTP activities deceased in smokers as compared to controls. We conclude, that even healthy, normolipidemic smokers have altered postprandial high density lipoprotein (**HDL**) cholesterol and apolipoprotein composition, as well as lipid transfer protein activities. The shift of cholesterol and apoE from **HDL** to the triglyceride-rich lipoprotein (TRL) fraction, together with decreased plasma apoA-I and LpA-I concentrations during alimentary lipemia may indicate impaired reverse cholesterol transport. Both the postprandial increase in TRL and the lowering of **HDL** may promote atherogenesis in smokers. PMID: 9684753, UI: 98347895

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

44: Arterioscler Thromb Vasc Biol 1998 May;18(5):833-41

No effect of consumption of green and black tea on plasma lipid and antioxidant levels and on LDL oxidation in smokers.

Princen HM, van Duyvenvoorde W, Buytenhek R, Blonk C, Tijburg LB, Langius JA, Meinders AE, Pijl H

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Intake of flavonoids is associated with a reduced cardiovascular risk. Oxidation of **LDL** is a major step in atherogenesis, and antioxidants may protect **LDL** from oxidation. Because tea is an important source of flavonoids, which are strong antioxidants, we have assessed in a randomized, placebo-controlled study the effect of consumption of black and green tea and of intake of isolated green tea polyphenols on **LDL** oxidation ex vivo and on plasma levels of antioxidants and lipids. Healthy male and female smokers (aged 34+/-12 years, 13 to 16 per group) consumed during a 4-week period 6 cups (900 mL) of black or green tea or water per day, or they received as a supplement 3.6 grams of green tea polyphenols per day (equivalent to the consumption of 18 cups of green tea per day). Consumption of black or green tea had no effect on plasma cholesterol and triglycerides, **HDL** and **LDL** cholesterol, plasma vitamins C and E, beta-carotene, and uric acid. No differences were found in parameters of **LDL** oxidation. Intake of green tea polyphenols decreased plasma vitamin E significantly in that group compared with the control group (-11% P=.016) but had no effect on **LDL** oxidation ex vivo. We conclude that consumption of black or green tea (6 cups per day) has no effect on plasma lipids and no sparing effect on plasma antioxidant vitamins and that intake of a high dose of isolated green tea polyphenols decreases plasma vitamin E. Although tea polyphenols had a potent antioxidant activity on **LDL** oxidation in vitro, no effect was found on **LDL** oxidation ex vivo after consumption of green or black tea or intake of a green tea polyphenol isolate. Publication Types: Clinical trial Randomized controlled trial PMID: 9598844, UI: 98258791

PM3000457346

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

45: Stroke 1998 May;29(5):913-7

Cigarette smoking and other risk factors for silent cerebral infarction in the general population.

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BACKGROUND AND PURPOSE: Silent cerebral infarctions (SCIs) have a prevalence between 10% and 40% in the transient ischemic attack population and have been associated with increased mortality and morbidity; however, little is known about the prevalence and risk factors for SCI in the general population. This report focuses on the role of cigarette **smoking** and other risk factors for SCI in the general population. METHODS: MRI scans were performed on 1737 participants selected from the general population as part of the Atherosclerosis Risk in Communities Study. **Smoking** status and other major cerebrovascular risk factors were assessed, and associations between **smoking** status and SCIs were established with the use of ANCOVA. RESULTS: Overall, the prevalence of SCI in this population aged 55 to 70 years was 11%. Cigarette **smoking** had an ordered association (P=0.029) with the presence of SCI, with the odds ratio (OR) of non**smoking** participants exposed to environmental tobacco smoke being 1.06 (95% confidence interval [CI], 0.64 to 1.75) times as great as for nonsmokers not exposed; the OR of past smokers was 1.16 (95% CI, 0.74 to 1.83) times greater, and the OR of current smokers was 1.88 (95% CI, 1.13 to 3.13) times greater. An increased prevalence was also noted among black, older, and hypertensive participants. CONCLUSIONS: This report is among the first to examine the risk factors for SCI in the general population and finds a relatively high overall prevalence (11%). There is an ordered relationship between increasing exposure to cigarette smoke and the presence of SCI that parallels the relationship between **smoking** and carotid atherosclerosis. The magnitude of the association with **smoking** is substantial compared with the effect of hypertension and other traditional cerebrovascular risk factors. The reduction in prevalence of SCI between current and past smokers and the trend that increased pack-years of **smoking** is related to increased prevalence of SCI are both additional arguments for **smoking** avoidance and cessation.

PMID: 9596234, UI: 98255673

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

46: Eur J Med Res 1998 Apr 8;3(4):189-93

The early cardiovascular toll of cigarette smoking in dyslipidaemic patients in the United Kingdom.

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Relationships between early cardiovascular risk at mean follow-up 1. 8 years and cigarette **smoking** status were investigated through analysis of data from participating clinics entered from 1981-1994 in the UK-Lipid Clinics Programme computerised database. Lipid profiles and new cardiovascular events were recorded for 3601 male, 4883 female human non-smokers mean age 44.7 and 53.1 years, 3077 male, 2275 female current smokers age 46.3 and 50.3 years and 7210 male, 4559 female age 49.2 and 53.3 years ever-smokers. Levels of triglycerides and total cholesterol increased across the gradient never/ex/current smoker, with a reverse gradient for **HDL**-cholesterol. Never-smokers were slightly lighter than other groups and males were younger, differences insufficient to explain the lipid variation. Minor differences in blood pressure between groups did not show this gradient and the development of new hypertension was not consistently related to **smoking** habits. In contrast the expression of newly-recorded cardiovascular disease was greater and in some categories doubled for current or ex-smokers in contrast with never-smokers. This survey emphasises first, the continuing inadequacy of stop-**smoking** support even at specialist clinics, second, that patients who give up **smoking** are to be congratulated and benefit in the long-term but third, that the change in status can be recent and classification as ex-smoker can conceal high short-term risk, for which lipid profiles may also be significant and justify priority attention in management.

PM3000457348

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

47: Diabetes Care 1998 Apr;21(4):516-7

Serum leptin levels in smokers with type 2 diabetes.

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OBJECTIVE: To elucidate the molecular mechanism of **smoking** cessation and its relationship to body weight gain, the effects of **smoking** on the serum levels of leptin were studied in Japanese patients with type 2 diabetes. RESEARCH DESIGN AND METHODS: The serum levels of leptin after an overnight fast in 37 adult male Japanese patients with type 2 diabetes (17 smokers and 20 nonsmokers) were assayed using radioimmunoassay. In addition, the serum leptin levels in four nondiabetic smokers were measured before and 2 weeks after quitting **smoking**. RESULTS: Smokers and nonsmokers did not differ in age, BMI, or levels of blood glucose and fasting insulin but did differ in **HDL** cholesterol levels (1.07 +/- 0.18 vs. 1.32 +/- 0.24 mmol/l for smokers and nonsmokers, respectively, P = 0.002). The mean serum leptin level of smokers did not differ from that of nonsmokers (3.8 +/- 1.9 vs. 3.8 +/- 1.6 ng/ml). The leptin level correlated with the fasting insulin level and BMI (r = 0.55 and 0.56, P < 0.001 and 0.001, respectively). The leptin levels in four heavy smokers showed no change after the subjects quit **smoking** (3.3 +/- 1.0 vs. 3.8 +/- 1.8 ng/ml, before and after quitting, respectively). CONCLUSIONS: Because **smoking** did not affect the leptin levels, the effects of quitting **smoking** on the fuel metabolism appear to be due to some other factors.

PM3000457349

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

48: J Cardiovasc Risk 1997 Aug;4(4):279-81

The interrelationship among tobacco consumption, high-density lipoprotein cholesterol and leukocyte counts.

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BACKGROUND: Tobacco consumption is a major cardiovascular risk factor that has been related to changes in lipoprotein levels and in the leukocyte count. OBJECTIVE: To investigate the interrelationship among leukocytes, high-density lipoprotein (**HDL**) cholesterol levels and tobacco consumption. METHODS: In total 1022 healthy male miners aged 40.5+/-8 years (mean+/-SD) were evaluated consecutively during the period 1993-1994. We evaluated the **smoking** history of all of the subjects by means of a structured questionnaire. After the subject had fasted for 12 h we extracted blood samples by venepuncture. Plasma concentrations of **HDL** were determined enzymatically (by the CHOD-PAP method) and the leukocyte count was determined with an automatic analyser. Statistical analysis was performed using analysis of variance for the mean differences and the Pearson and stepwise tests to determine correlations. RESULTS: The leukocyte count was significantly lower (8.014+/-2.327/mm3, P < 0.05) in those subjects with levels of **HDL** cholesterol equal to or greater than 0.9 mmol/l in comparison with that in those with **HDL** cholesterol levels lower than 0.9 mmol/l (8.450+/-2.375/mm3). Leukocyte counts were correlated directly to tobacco consumption (r= 0.3119, P < 0.01) and inversely to H DL cholesterol levels (r = -0.1513, P < 0.01). **HDL** cholesterol levels were lower in smokers (1.15+/-0.31 mmol/l) and these differences were significant with respect to the levels in non-smokers (1.22+/-0.30 mmol/l, P<0.05) but not with respect to those in former smokers (1.21+/-0.39 mmol/l). The leukocyte count was significantly greater in smokers (8.963+/-2.428/mm3, P<0.05) than it was in former smokers (7.041+/-1.698/mm3) and in non-smokers (6.793+/-1.599/mm3). CONCLUSIONS: The results of this study indicate that tobacco consumption is associated with lower **HDL** cholesterol levels and higher leukocyte counts. Leukocyte counts correlate positively to tobacco consumption and inversely to **HDL** cholesterol levels. Subjects with **HDL** cholesterol levels lower than 0.9 mmol/l present with leukocyte counts higher than those found in those with **HDL** cholesterol values equal to or greater than 0.9 mmol/l.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

49: Arterioscler Thromb Vasc Biol 1997 Nov;17(11):2576-88

Peroxidation of LDL from combined-hyperlipidemic male smokers supplied with omega-3 fatty acids and antioxidants.

Brude IR, Drevon CA, Hjermann I, Seljeflot I, Lund-Katz S, Saarem K, Sandstad B, Solvoll K, Halvorsen B, Arnesen H, Nenseter MS

Institute for Nutrition Research, University of Oslo, Norway.

The effects of marine omega-3 polyunsaturated fatty acids (FAs) and antioxidants on the oxidative modification of **LDL** were studied in a randomized, double-blind, placebo-controlled trial. Male smokers (n = 41) with combined hyperlipidemia were allocated to one of four groups receiving supplementation with omega-3 FAs (5 g eicosapentaenoic acid and docosahexaenoic acid per day), antioxidants (75 mg vitamin E, 150 mg vitamin C, 15 mg beta-carotene, and 30 mg coenzyme Q10 per day), both omega-3 FAs and antioxidants, or control oils. **LDL** and human mononuclear cells were isolated from the patients at baseline and after 6 weeks of supplementation. **LDL** was subjected to cell-mediated oxidation by the patients' own mononuclear cells, as well as to Cu(2+)-catalyzed and 2,2'-azobis-(2-amidinopropane hydrochloride) (AAPH)-initiated oxidation. Extent of **LDL** modification was measured as lag time, the formation rate of conjugated dienes (CDs), the maximum amount of CDs formed, formation of lipid peroxides, and the relative electrophoretic mobility of **LDL** on agarose gels. Dietary supplementation with omega-3 FAs increased the concentration of total omega-3 FAs in **LDL** and reduced the concentration of vitamin E in serum. The omega-3 FA-enriched **LDL** particles were not more susceptible to Cu(2+)-catalyzed, AAPH-initiated, or autologous cell-mediated oxidation than control **LDL**. In fact, enrichment with omega-3 FAs significantly reduced the formation rate of CDs when **LDL** was subjected to AAPH-induced oxidation. Supplementation with moderate amounts of antioxidants significantly increased the concentration of vitamin E in serum and increased the resistance of **LDL** to undergo Cu(2+)-catalyzed oxidation, measured as increased lag time, reduced formation of lipid peroxides, and reduced relative electrophoretic mobility compared with control **LDL**. Supplementation with omega-3 FAs/antioxidants showed oxidizability of **LDL** similar to that of control **LDL** and omega-3 FA-enriched **LDL**. In conclusion, omega-3 FAs neither rendered the **LDL** particles more susceptible to undergo in vitro oxidation nor influenced mononuclear cells' ability to oxidize autologous **LDL**, whereas moderate amounts of antioxidants protected **LDL** against oxidative modification.

Publication Types:
Clinical trial
Randomized controlled trial

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

50: Am J Physiol 1997 Oct;273(4 Pt 2):H1644-50

Endothelium-dependent vasodilation in the brachial artery is impaired in smokers: effect of vitamin C.

Motoyama T, Kawano H, Kugiyama K, Hirashima O, Ohgushi M, Yoshimura M, Ogawa H, Yasue H

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Cigarette **smoking** has been shown to cause endothelial dysfunction. To examine the effects of vitamin C and cigarette **smoking** on endothelium-dependent vasodilation, we measured the lumen diameter and flow velocity of the brachial arteries at rest, during reactive hyperemia following transient arterial occlusion, and after sublingual nitroglycerin (0.3 mg) in smokers (n = 20) and nonsmokers (n = 20) with high-resolution ultrasound after infusion of saline or saline plus vitamin C (10 mg/min for 20 min). We also performed the same study in smokers (n = 15) before and 10 min after cigarette **smoking**. In addition, we measured the serum levels of vitamin C and the plasma levels of thiobarbituric acid-reactive substances (**TBARS**) as an index of lipid peroxidation. The smokers had lower vitamin C levels, higher **TBARS** levels, and showed impairment of flow-dependent vasodilation (5.3 +/- 1.9 vs. 9.2 +/- 1.5%, P < 0.0001) compared with nonsmokers. Vitamin C administration improved the impairment of flow-dependent vasodilation (5.3 +/- 1.9 to 9.0 +/- 3.2%, P < 0.001) and decreased **TBARS** in smokers but not in nonsmokers. Furthermore, cigarette **smoking** acutely worsened the impairment of flow-dependent vasodilation (5.4 +/- 1.8 to 1.5 +/- 1.3%, P < 0.01) and increased **TBARS**. We conclude that 1) endothelium-dependent vasodilation in the brachial arteries is impaired in smokers and this impairment is improved by vitamin C administration in association with a decrease in **TBARS** and 2) cigarette **smoking** produces acute impairment of endothelium-dependent vasodilation in smokers in association with an increase in **TBARS**.

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51: Clin Chim Acta 1997 Sep 8;265(1):1-12
Low and very low density lipoprotein composition and resistance to copper-induced oxidation are not notably modified in smokers.

Marangon K, Herbeth B, Artur Y, Esterbauer H, Siest G

Centre de Medecine Preventive, Vandoeuvre-les-Nancy, France.

To study whether tobacco use was associated with oxidative phenomena affecting lipoproteins, we estimated susceptibility of **LDL** and V**LDL** to an in vitro copper-mediated oxidation, and measured serum autoantibody titers against oxidized **LDL** in 45 middle-age healthy nonsmokers, 35 smokers and 37 ex-smokers of both sexes, taking into account the detailed lipid composition of the lipoproteins. V**LDL** from female smokers had higher triglyceride, phospholipid, apolipoprotein E and alpha-tocopherol content and showed a higher rate of copper-induced oxidation in comparison with those from nonsmokers (P < or = 0.05) whereas the relative composition of these particles in saturated, mono- or poly-unsaturated fatty acids was not modified by tobacco consumption. After adjustment for triglyceride content, no statistically significant difference in oxidation rate was observed. Lipid, alpha-tocopherol and protein composition of **LDL** did not appear to be influenced by **smoking**; in accordance with these observations, no difference in indices of in vitro oxidizability of **LDL** was noticed between the different groups. Autoantibody titers against ox**LDL** were similar in smokers and nonsmokers. We conclude that, in supposed healthy individuals, **smoking** does not seem to be associated with notable variations in composition of V**LDL** and **LDL** or with an increase of oxidizability of these atherogenic lipoproteins.

52: Jpn Heart J 1997 Jul;38(4):497-502
The effect of cigarette smoking during pregnancy on cord blood lipid, lipoprotein and apolipoprotein levels.

Iscan A, Yigitoglu MR, Ece A, Ari Z, Akyildiz M
Department of Pediatrics, Faculty of Medicine, University of Celal Bayar, Manisa, Turkey.

We examined the relationship between maternal **smoking** during pregnancy and serum lipid, lipoprotein and apolipoprotein levels in newborns. Serum concentrations of total cholesterol, triglyceride, high density lipoprotein cholesterol, low density lipoprotein cholesterol, apolipoprotein A-1, apolipoprotein B and lipoprotein (a) were assessed in blood samples from 38 mothers who were smokers and their newborns obtained at delivery and compared to blood sample from 42 nonsmokers and their newborns. As compared with newborns of nonsmoker mothers, newborns of smoker mothers showed a lower mean level of high density lipoprotein cholesterol (21 versus 26 mg/dl, $p < 0.01$), a higher total cholesterol to high density lipoprotein cholesterol (4.7 versus 3.7, $p < 0.01$), a higher low density lipoprotein cholesterol to high density lipoprotein cholesterol ratios (3.2 versus 2.3, $p < 0.05$), a lower mean level of apolipoprotein A-1 (105 versus 129 mg/dl, $p < 0.01$) and a higher apolipoprotein B to apolipoprotein A-1 ratio (0.44 versus 0.3, $p < 0.01$). These parameters were also different between smoker and nonsmoker mothers. There were no significant differences in TC, TG, **LDL**-C, Apo B and Lp (a) values between the two newborn groups. These data suggest that maternal **smoking** during pregnancy markedly affects lipid metabolism in the fetus.

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Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

53: Eur J Clin Nutr 1997 Sep;51(9):601-6

Effect of increased fruit and vegetable intake on the susceptibility of lipoprotein to oxidation in smokers.

Hininger I,Chopra M, Thurnham DI, Laporte F, Richard MJ, Favier A, Roussel AM

GREPO, Universite Joseph Fourier, La Tronche, France.

OBJECTIVE: To evaluate the effect of an increased dietary intake of fruit and vegetables on susceptibility of **LDL** to oxidation in smokers and nonsmokers. DESIGN: A descriptive and prospective study. SETTING: Joseph Fourier University, Grenoble. SUBJECTS: Volunteers were age and sex matched in the **smoking** and non**smoking** groups and were recruited by announcement. INTERVENTIONS: Increased intake of fruits and vegetables for two weeks providing 30 mg/day of carotenoids. MAIN OUTCOME MEASURES: Circulating levels of beta-carotene, lutein, lycopene, alpha-tocopherol; susceptibility of **LDL** to oxidation. Cu-Zn superoxide dismutase (Cu-Zn SOD), and Se glutathione peroxidase (Se-GSH-Px) activities and reduced (GSH) and oxidized (GSSG) glutathione. RESULTS: At entry (week 0: W0) smokers exhibited a lower plasma carotene level but the plasma parameters of oxidative stress and **LDL** oxidizability were not different from nonsmokers. After two weeks of increased intake of fruits and vegetables the circulating levels of carotenoids increased in smokers 23% and 11% in nonsmokers. At the same time the resistance of **LDL** to oxidation increased by 14% in smokers ($P <$ or $= 0.05$) and by 28% in nonsmokers ($P <$ or $= 0.025$). The mean whole blood GSH level was higher in smokers at entry but returned to a concentration similar to nonsmokers at the end of the study. CONCLUSION: This pilot study indicates that an increased, carotenoid rich food intake through its inhibitory effect on the susceptibility of **LDL** to oxidation may be an interesting approach to reduce the risk of atherosclerosis both in smokers and nonsmokers.

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54: Circulation 1997 Oct 7;96(7):2128-36
The Munster Heart Study (PROCAM): total mortality in middle-aged men is increased at low total and LDL cholesterol concentrations in smokers but not in nonsmokers.

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BACKGROUND: Some large epidemiological studies have shown an increase in mortality at low levels of total and **LDL** cholesterol. It has been speculated that low cholesterol levels may play a causative role in this association. To investigate this question, we analyzed all deaths occurring among middle-aged men in the Munster Heart Study (PROCAM), one of the largest prospective epidemiological studies of coronary heart disease risk markers in Europe. METHODS AND RESULTS: In the Munster Heart Study, 10,856 men aged 36 to 65 years at study entry (46.8+/-7.3 years [mean+/-SD]) were followed for 4 to 14 years (7.1+/-2.4 years). During this period, 313 deaths occurred--46 from myocardial infarction, 48 from suspected or definite sudden cardiac death, 14 from cerebrovascular disease, and 10 from other diseases of the circulatory system. There were 121 deaths from cancer and 33 deaths from violent causes (injuries in 16, suicide in 14, and homicide in 3 cases). Death in 29 cases occurred from other causes and was unexplained in 12 cases. Total cholesterol, **LDL** cholesterol, and the **LDL/HDL** ratio showed a J-shaped relationship with total mortality. At high total and **LDL** cholesterol concentrations, increased mortality was due to increased coronary deaths. At low total and **LDL** cholesterol concentrations, increased mortality was seen in smokers only and was explained by an increase in **smoking**-related cancer deaths. CONCLUSIONS: The increase in mortality at low levels of total and **LDL** cholesterol among middle-aged men in the Munster Heart Study is explained by an increase in **smoking**-related cancer deaths among smokers.

Publication Types:
Multicenter study

55: Circulation 1997 Aug 19;96(4):1097-101
Association between cigarette smoking and lipid peroxidation in a controlled feeding study.

Miller ER 3rd, Appel LJ, Jiang L, Risby TH

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BACKGROUND: Cigarette smoke may promote atherogenesis by producing oxygen-derived free radicals that damage lipids. However, evidence in support of this hypothesis is inconsistent because most studies did not control for aspects of diet (antioxidants and lipid substrate) that may confound the association between **smoking** and measures of lipid peroxidation. METHODS AND RESULTS: The relationships between cigarette **smoking** and two measures of lipid peroxidation, breath ethane (an in vivo assay) and thiobarbituric acid-

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reactive substances (**TBARS**, an in vitro assay), were examined in 123 adults (11% of whom were smokers) participating in a controlled feeding study. After 3 weeks of controlled feeding on a common diet (36% total fat, 14% saturated fats, 6% polyunsaturated fats, and 12% monounsaturated fats), breath and fasting serum samples were collected for measurement of ethane and **TBARS**, respectively. Baseline characteristics of smokers and nonsmokers were similar, including several indices related to diet and nutritional status (albumin, cholesterol, body mass index, and oxygen radical-absorbing capacity). Cigarette smokers had significantly higher breath ethane (8.88 versus 1.71 pmol/L; P<.0001) and **TBARS** (24.0 versus 20.7 micromol/mL; P=.008) than nonsmokers. The interval between breath collection and the time the last cigarette was smoked was significantly and inversely correlated with breath ethane. Neither measure of lipid peroxidation was associated with measures of serum cholesterol or albumin, body mass index, or serum oxygen radical-absorbing capacity. CONCLUSIONS: Cigarette smokers have higher rates of in vivo and in vitro lipid peroxidation. These results support the hypothesis that the atherogenic effects of **smoking** are mediated in part by free radical damage to lipids.
Publication Types:
Clinical trial

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

56: Free Radic Res 1997 Jul;27(1):105-12

alpha-Tocopherol binding activity of red blood cells in smokers.

Bellizzi MC, Dutta-Roy AK, Duthie GG, James WP

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Despite high plasma levels of vitamin E, red blood cell membranes contain relatively low levels of vitamin E. This suggests the existence of a selective vitamin E uptake/regeneration system in human red blood cell membranes. alpha-Tocopherol binding sites on human red blood cells are thought to be involved in the uptake of alpha-tocopherol from the plasma. To understand the role of the uptake system we have compared the alpha-tocopherol content and binding activity of red blood cells from smokers and non-smokers. The specific binding of [3H] alpha-tocopherol to pure red blood cell preparations from smokers (n = 7, 28.4 +/- 2.8 years) was 30.6 +/- 3.2 fmoles per 3 x 10(8) red blood cells and for non-smokers (n = 17, 27.9 +/- 1.3 years) was 41.7 +/- 3.7 fmoles per 3 x 10(8) red blood cells. Thus alpha-tocopherol uptake activity was significantly lower in smokers (P = 0.05). Red blood cells from smokers contained less (1.8 +/- 0.4 micrograms/gHb) alpha-tocopherol than non-smokers (2.8 +/- 0.3 micrograms/gHb), (P < 0.05), despite plasma levels of alpha-tocopherol being similar: 12.9 +/- 0.8 microM in non-smokers vs. 12.7 +/- 0.5 microM in smokers. However, adjusting plasma alpha-tocopherol for total plasma cholesterol plus triacylglycerols showed alpha-tocopherol levels were higher (P < 0.01) in non-smokers (2.84 +/- 0.10 mumol alpha-tocopherol/ mmol [cholesterol+triacylglycerol]) than in smokers (2.36 +/- 0.11 mumol alpha-tocopherol/mmol [cholesterol+triacylglycerol]). The reduced alpha-tocopherol levels in red blood cells from smokers may be due to impairment of alpha-tocopherol uptake activity. The reduced levels of alpha-tocopherol in smokers red blood cells was not associated with any changes in cell membrane fluidity. At present it is not known whether supplementation of smokers with vitamin E would normalise the alpha-tocopherol uptake activity of red blood cells.

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Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

57: Eur J Clin Nutr 1997 Jul;51(7):472-7

The effect of ascorbic acid on plasma lipids and oxidisability of LDL in male smokers.

Samman S, Brown AJ, Beltran C, Singh S

Department of Biochemistry, University of Sydney, NSW, Australia.

OBJECTIVE: The aims of this study were to investigate the effect of ascorbic acid (AA) supplementation on the oxidisability of low density lipoprotein (**LDL**) in vitro and on plasma lipoproteins under controlled dietary conditions. DESIGN: Randomised single-blind cross-over trial. SETTING: Free living subjects. SUBJECTS: Eight male smokers (age: 25 +/- 2.4 y, BMI: 20.7 +/- 0.5, cigarettes per day: 19.1 +/- 2.4; means +/- s.e.). INTERVENTIONS: Dietary intake was determined in all subjects were advised to achieve an intake as close as possible to the recommended dietary intake of AA (40 mg). After two weeks on the baseline diet, subjects were asked to consume 1 g AA per day for two weeks followed by two weeks of placebo supplementation, or vice versa. In view of the carry-over effects of plasma AA, a wash-out period was incorporated between treatments. Duplicate venous blood samples were collected before and after supplementation and the plasma concentrations of AA, lipids and lipoproteins were determined. The in vitro copper-induced oxidisability of **LDL** was assessed by monitoring of the absorbance of 234 nm. RESULTS: No changes in the plasma lipids or the oxidisability of **LDL** were found after AA supplementation compared to placebo. Plasma AA concentrations doubled on average after supplementation indicating that the lack of effect was not a result of poor compliance. CONCLUSIONS: AA supplementation at this dose did not alter plasma lipids of **LDL** oxidisability in male smokers.

Publication Types:
Clinical trial
Randomized controlled trial

PM3000457358

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

58: Metabolism 1997 Jun;46(6):711-5
Effect of smoking cessation on lipoprotein A-I and lipoprotein A-I:A-II levels.

Richard F, Marecaux N, Dallongeville J, Devienne M, Tiem N, Fruchart JC, Fantino M, Zylberberg G, Amouyel P

Contrat Jeune Formation Institut National de la Sante et de la Recherche Medicale (INSERM) 95-05, Service d'Etude et de Recherche sur les Lipoproteines et l'Atherosclerose, Lille, France.

Cigarette **smoking** is associated with low plasma high-density lipoprotein cholesterol (**HDL**-C) and apolipoprotein (apo) A-I levels, which may explain, in part, its deleterious effects on coronary heart disease (CHD). In a group of ex-smokers, we assessed the influence of **smoking** cessation on apo A-I particle levels. Plasma lipid, apolipoprotein, and lipoparticle concentrations of 58 subjects who had completely stopped **smoking** (ex-smokers) were compared with those of 37 subjects who had continued **smoking** (smokers) before and after a **smoking** cessation counseling program. Nutritional intake was recorded before and after the program to adjust for potential interaction with plasma lipid variables. Smokers and ex-smokers were similar in gender distribution, age, body mass index (BMI), social status, and nutrient intake. There were significantly greater increases in total cholesterol ($P < .04$), **HDL**-C ($P < .005$), **HDL**2-C ($P < .008$), and lipoprotein (Lp) A-I:A-II ($P < .04$) in ex-smokers than in smokers. After **smoking** cessation, ex-smokers consumed more vegetable protein ($P < .02$) and polysaccharides ($P < .04$) and had higher plasma levels of **HDL**-C ($P < .0004$), apo A-I ($P < .001$), Lp A-I ($P < .007$), and Lp A-I:A-II ($P < .01$) than smokers. Adjustments on nutritional variables did not show any additional difference between ex-smokers and smokers, suggesting that **smoking** per se effects Lp A-I and Lp A-I:A-II levels. In conclusion, **HDL** particles including Lp A-I and Lp A-I:A-II are higher in ex-smokers than in smokers.

59: Eur J Clin Invest 1997 May;27(5):450-6
Smoking cessation improves insulin sensitivity in healthy middle-aged men.

Eliasson B, Attvall S, Taskinen MR, Smith U
Lundberg Laboratory for Diabetes Research, Department of Medicine, Sahlgrenska University Hospital, Goteborg, Sweden.

Cigarette smokers have recently been shown to exhibit insulin resistance, dyslipidaemia and markers of the insulin resistance syndrome (IRS). The aim of this study was to examine the effects of **smoking** cessation on insulin sensitivity and IRS. Forty male, non-obese healthy smokers participated in this open parallel study with 8 weeks of follow-up. Seventeen subjects were able to stop **smoking**, while 23 subjects continued to smoke and served as a controls group. Anthropometric and metabolic data were measured. Degree of insulin sensitivity was determined with the euglycaemic hyperinsulinaemic clamp technique. **Smoking** cessation increased insulin sensitivity and improved the lipoprotein profile in spite of a modest increase in body weight. Initial **smoking** habits correlated positively with the increase in BMI as well as the improvements in the metabolic variables after **smoking** cessation. These data support the view that **smoking** causes insulin resistance and IRS, and also demonstrate that the beneficial metabolic effects of **smoking** cessation override the effects of an accompanying modest increase in body weight.

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Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

60: N Engl J Med 1997 May 1;336(18):1276-82

Coronary risk factors and plaque morphology in men with coronary disease who died suddenly.

Burke AP, Farb A, Malcom GT, Liang YH, Smialek J, Virmani R

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BACKGROUND: Cigarette **smoking** and abnormal serum cholesterol concentrations are risk factors for acute coronary syndromes, but the underlying mechanisms are poorly understood. We studied whether cigarette **smoking** and abnormal cholesterol values may precipitate acute coronary thrombosis and sudden death resulting from either rupture of vulnerable coronary plaques or erosion of plaques. METHODS: We examined the hearts of 113 men with coronary disease who had died suddenly and also analyzed their coronary risk factors. We found an acute coronary thrombus in each of 59 men, and severe narrowing of the coronary artery by an atherosclerotic plaque without acute thrombosis (stable plaque) in 54. Cases of acute thrombosis were divided into two groups: 41 resulting from rupture of a vulnerable plaque (a thin fibrous cap overlying a lipid-rich core), and 18 resulting from the erosion of a fibrous plaque rich in smooth-muscle cells and proteoglycans. Vulnerable plaques that had not ruptured were counted in each heart. RESULTS: Cigarette **smoking** was a risk factor in 44 (75 percent) of the men with acute thrombosis, as compared with 22 (41 percent) of the men with stable plaques (P<0.001). The mean (+/-SD) ratio of serum total cholesterol to high-density lipoprotein (**HDL**) cholesterol was markedly elevated in the men who died of acute thrombosis with plaque rupture (mean, 8.5+/-4.0) but only mi**LDL**y elevated in the men without acute thrombosis (5.5+/-2.4; P<0.001) and in the men with thrombi overlying eroded plaques (5.0+/-1.8; P<0.001). Multivariate analysis showed an association between an elevated ratio of serum total cholesterol to **HDL** cholesterol and the presence of vulnerable plaques (P<0.001). CONCLUSIONS: Among men with coronary disease who die suddenly, abnormal serum cholesterol concentrations - particularly elevated ratios of total cholesterol to **HDL** cholesterol - predispose patients to rupture of vulnerable plaques, whereas cigarette **smoking** predisposes patients to acute thrombosis.

Comments:
Comment in: N Engl J Med 1997 May 1;336(18):1312-4

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

61: Atherosclerosis 1997 Mar 21;129(2):169-76

Plasma levels of lipid and cholesterol oxidation products and cytokines in diabetes mellitus and cigarette smoking: effects of vitamin E treatment.

Mol MJ, de Rijke YB, Demacker PN, Stalenhoef AF

Department of Medicine, University Hospital Nijmegen, Netherlands.

To evaluate the role of both oxidation and inflammation in atherosclerosis, we compared **LDL** oxidizability, in vivo lipid and cholesterol oxidation, and basal and lipopolysaccharide (LPS)-stimulated production of various cytokines in normolipidemic patients with diabetes mellitus (DM: n = 11), cigarettes smokers (n = 14). In addition, the effects of vitamin E (600 I.U./day for 4 weeks) on these parameters were evaluated. Initial **LDL** oxidation characteristics before and after vitamin E were identical in the 3 groups. Plasma thiobarbituric acid reactive substances were higher in DM and smokers versus controls (0.77 +/- 0.22, 0.74 +/- 0.14 versus 0.62 +/- 0.10 mumol **malondialdehyde** equivalents/l, respectively; P versus controls < 0.05) and normalized after vitamin E supplementation. Total plasma oxysterols were higher in smokers versus controls (354 +/- 104 versus 265 +/- 66 nmol/l, P < 0.05) and unaffected by vitamin E. The basal and LPS-stimulated levels of interleukin-1 beta and tumour necrosis factor alpha (TNF alpha) and the basal level of interleukin-1-receptor antagonist (IL-1RA) were identical for the 3 groups. LPS-stimulated IL-1RA was higher in DM versus controls (10.7 +/- 2.0 versus 8.1 +/- 1.7 pmol/l, P < 0.05). After vitamin E, TNF alpha dropped in controls and smokers, and IL-1RA in smokers only. Results suggest increased in vivo oxidative stress and inflammation in DM and **smoking**, which is partly overcome by vitamin E.

62: An Esp Pediatr 1997 Mar;46(3):245-51

[Distribution of lipidic values in teenagers that smoke].

[Article in Spanish]

Palau Bondia J, Reparaz Abaitua F, Elcarte Lopez R, Inigo Martinez J, Ferreiro Mazon H, Aldaz Izurzu Y, Villa Elizaga I

Servicio de Pediatria, Hospital Virgen del Camino, Pamplona.

OBJECTIVE: To determine the lipidic profiles in a population of teenagers and determine their relationship with **smoking**. PATIENTS AND METHODS: We have studied 910 teenagers, between 14 and 17 years of age. Information regarding **smoking** was obtained with a questionnaire. Serum levels of cholesterol, **HDL**, **LDL**, triglycerides, apoprotein A and apoprotein B were measured by enzymatic methods. RESULTS: Total cholesterol of non-smokers is higher than in smokers. Even if we divide the population studied by gender, the difference remain. Nevertheless, smokers' mean **HDL** level is lower, especially in boys. The **LDL/HDL** index is slightly higher in smokers than in non-smokers. However, if we separate boys and girls, we found some differences. Boys that smoke have higher cholesterol/**HDL** and **LDL/HDL** than non-**smoking** boys. Adjusting lipidic values by body mass, age and triglyceride serum levels, the relationship between **smoking** and lower cholesterol, **HDL** and apoprotein A and higher serum triglyceride levels remains in boys.

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Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

63: Eur J Clin Nutr 1997 Mar;51(3):154-63

Effect of supplementation of smoking men with plain or slow release ascorbic acid on lipoprotein oxidation.

Nyyssonen K, Poulsen HE, Hayn M, Agerbo P, Porkkala-Sarataho E, Kaikkonen J, Salonen R, Salonen JT

Research Institute of Public Health, University of Kuopio, Finland.

OBJECTIVE: To study the effects of two month ascorbic acid supplementation on in vitro lipoprotein oxidation resistance and on in vivo lipid peroxidation, and to compare the absorption of two ascorbic acid preparations. DESIGN: Randomized, single blinded and placebo-controlled clinical trial. SETTING: Men, aged 36-65 y, **smoking** 11-40 cigarettes daily. SUBJECTS: Sixty-two subjects were recruited by newspaper advertisements and randomized. Fifty-nine subjects completed the study. INTERVENTION: Subjects were randomized into three groups to receive 250 mg BID of plain or slow release ascorbic acid tablets or placebo daily for two months. In the pharmacokinetic part of the study, the absorption of the ascorbic acid preparations was followed for 12 h. MAIN OUTCOME MEASURES: Plasma **malondialdehyde** (MDA) concentration and the oxidation resistance of **VLDL** + **LDL**. For the pharmacokinetic study, the area under the plasma concentration curve (AUC) of ascorbic acid. RESULTS: Plasma reduced ascorbic acid increased by 32% in the plain ascorbate group and by 54% in the slow release group during a two month supplementation. Plasma MDA increased in the plain ascorbic acid group compared with placebo group ($P < 0.05$), but there were no significant differences in the changes in lipoprotein oxidation reactions induced by copper or by hemin and H_2O_2. Plasma reduced and total ascorbic acid AUC values were significantly higher in both plain and slow release ascorbate groups compared with placebo group. CONCLUSIONS: Oral supplementation of 500 mg of ascorbic acid daily for two months alone without any other antioxidant does not appear to have protective effect on either in vitro lipoprotein oxidation resistance or in vivo lipid peroxidation in **smoking** men, but might even promote the formation of MDA.

Publication Types:
Clinical trial
Randomized controlled trial

PM3000457362

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

64: J Intern Med 1997 Feb;241(2):157-63
Alcohol and coronary heart disease: the roles of HDL-cholesterol and smoking.

Manttari M, Tenkanen L, Alikoski T, Manninen V

Department of Medicine, Helsinki University, Finland.

OBJECTIVES: To study the role of **HDL**-cholesterol (**HDL**c) in the causal pathway mediating the effect of alcohol on coronary heart disease (CHD). DESIGN: Cox proportional hazard models were used to compare the relative CHD risks in various **HDL**c-**smoking** categories. SETTING: A prospective, multicentre, placebo-controlled, double-blind CHD primary prevention trial with gemfibrozil in primary (occupational) health care units, the Helsinki Heart Study. SUBJECTS: Dyslipidaemic middle-aged men with available alcohol consumption data (1924 of 2035) in the placebo arm of the 5-year study. MAIN OUTCOME MEASURES: Seventy-seven (of 84) cases of nonfatal myocardial infarction or cardiac death. RESULTS: A U-shaped association was detected between alcohol consumption and CHD. The protection was found both in subjects with low (mean 0.94 mmol L-1) and normal (mean 1.25 mmol L-1) **HDL**c with corresponding reductions of 23% and 36% in relative risks. In contrast to previous data, alcohol offered virtually no protection against CHD in non-smokers. In subjects consuming more than 800 g pure ethanol annually, the CHD incidence was 6/1000 in subjects with more than three weekly drinking occasions, compared to 11/1000 in 'weekend' drinkers. CONCLUSIONS: Our results confirm the protective effect of alcohol against CHD. However, in contrast to previous data the effect in our population is restricted to smokers and the role of **HDL**c in mediating the effect is less central than suggested previously.
Publication Types:
Clinical trial
Multicenter study
Randomized controlled trial

65: Acta Oncol 1997;36(2):137-40
Hormone-metabolic status in moderately smoking breast cancer patients.

Berstein LM, Tsyrlina EV, Semiglazov VF, Kovalenko IG, Gamayunova VB, Evtushenko TP, Ivanova OA

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One hundred and eighteen primary breast cancer (BC) patients, 35 of whom were smokers, in clinical stages I-II of the disease were examined. In order to investigate whether **smoking** changes endocrine function in BC patients, some indices of the hormone-metabolic status of **smoking** and non-**smoking** patients of reproductive and menopausal age were compared. It was found that in smokers with BC there was a decline in body weight and body fat content, a lack of lean body mass accumulation along with body mass increase, a tendency to hypotriglyceridemia and hypoinsulinemia, accelerated development of the upper type of body fat distribution with ageing, intensified gonadotropin secretion, shifts in steroidogenesis and SHBG level and elevated catecholamine execretion. It is suggested that a possible relation between hormone-mediated effects inherent to **smoking** and the mechanisms promoting genotoxic type of hormonal carcinogenesis and the factors of breast cancer prognosis cannot be excluded.

PM3000457363

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

66: Epidemiology 1997 Jan;8(1):48-54
Is cigarette smoking an effect modifier of the relation between antihypertensive therapy and blood lipids?
Derby CA, Lapane KL, Hume AL, Babour MM, Carleton RA

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We examined the relation between current use of antihypertensive medications and lipid levels in relation to **smoking** status. We used data from cross-sectional random sample surveys conducted between 1981 and 1993 in two southeastern New England communities. The analysis included 3,027 normotensive, 1,416 untreated hypertensive, and 1,174 treated hypertensive survey respondents between 40 and 64 years of age. After adjustment for body mass index, diabetes, mellitus, alcohol use, use of medications with adverse lipid effects, age, and sex, the estimated mean high-density-lipoprotein-cholesterol level among hypertensives using beta-blockers [44.6 mg per dl; 95% confidence interval (CI) = 43.1-46.1] was lower than that for either hypertensives (48.5 mg per dl; 95% CI = 47.8-49.2) or normotensives (47.1 mg per dl; 95% CI = 46.6-47.6). This pattern was similar among smokers and nonsmokers. Smokers treated with beta-blockers, however, had particularly low levels of high-density-lipoprotein-cholesterol (43.4 mg per dl; 95% CI = 40.7-46.1), compared with non-smokers using beta-blockers (45.8 mg per dl; 95% CI = 44.2-47.3). Low levels of high-density-lipoprotein-cholesterol may increase the risk of coronary heart disease among smokers using beta-blockers.

67: J Natl Med Assoc 1997 Jan;89(1):37-47
Coronary heart disease risk factors and cigarette smoking among rural African Americans.

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Cigarette **smoking** has been reported to worsen high-density lipoprotein (**HDL**) cholesterol and other cardiac risk factors, yet no studies have examined this issue among rural African Americans. This study examines the association between cigarette **smoking** and cardiac risk factors among rural African Americans. A population-based sample of 403 African-American adults from two rural Virginia counties underwent total cholesterol (TC), **HDL**, systolic and diastolic blood pressure (SBP and DBP), body mass index (BMI), serum glucose, and glycosylated hemoglobin (GlyHb) measurements. Cross-sectional multivariate analyses were used to compare risk factors across categories of cigarette use. Age, BMI, alcohol consumption, and the use of antihypertensive medications were covariates in the analysis. Results indicated that female light smokers had significantly lower SBP and DBP, and lower **HDL**. Female heavy smokers had significantly lower **HDL** and BMI and significantly higher TC/**HDL** ratios. Male heavy smokers had significantly higher SBP. More than 33% of males and more than 50% of females were overweight, and increasing BMI was associated with significantly or nearly significantly worsening of all other risk factor levels. Both cigarette **smoking** and obesity adversely affect other cardiac risk factors. Novel approaches are needed to decrease both **smoking** and obesity in this difficult to reach population.

PM3000457364

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

68: J Appl Physiol 1996 Nov;81(5):2053-9

Cigarette smoke-induced bronchoconstriction: causative agents and role of thromboxane receptors.

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Inhalation of cigarette smoke induces a biphasic bronchoconstriction in guinea pigs: the first phase is induced by a combination of cholinergic reflex and tachykinins, whereas the second phase involves cyclooxygenase metabolites (J.-L. Hong, I. W. Rodger, and L.-Y. Lee. J. Appl. Physiol. 78: 2260-2266, 1995). This study was carried out to further determine the causative agents in the smoke and the types of prostanoid receptors and endogenous prostanoids mediating the bronchoconstriction. Inhalation of 10 ml of high-nicotine cigarette smoke consistently elicited the biphasic bronchoconstriction in anesthetized and artificially ventilated guinea pigs. Pretreatment with hexamethonium (10 mg/kg iv) significantly reduced the first-phase bronchoconstriction but did not have any measurable effect on the second-phase response. In sharp contrast, gas-phase smoke did not elicit any bronchoconstrictive effect. Furthermore, when the animals were challenged with low-nicotine cigarette smoke, only a single second-phase response was evoked, accompanied by increases in **thromboxane (Tx) B2** (a stable metabolite of TxA2), prostaglandin (PG) D2, **PGF2** alpha in the bronchoalveolar lavage fluid. The bronchoconstrictive response induced by low-nicotine smoke was completely prevented by pretreatment with SQ-29548 (0.3 mg/kg iv), a TxA2-receptor antagonist. These results indicate that 1) nicotine is the primary causative agent responsible for the first-phase bronchoconstriction and 2) nonnicotine smoke particulates evoke the release of TxA2, PGD2, and **PGF2** alpha, which act on TxA2 receptors on airway smooth muscles and induce the second-phase response to cigarette smoke.

PM3000457365

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69: Diabetes Care 1996 Nov;19(11):1233-6

Increase in circulating products of lipid peroxidation in smokers with IDDM.

Zoppini G, Targher G, Monauni T, Faccini G, Pasqualini E, Martinelli C, Zenari ML, Muggeo M

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OBJECTIVE: To measure plasma **malondialdehyde** (MDA) concentration, a product of lipid peroxidation, both in IDDM patients and in healthy control subjects and to examine whether **smoking** has a negative impact on the plasma **MDA** levels in diabetic patients. RESEARCH DESIGN AND METHODS: Plasma total MDA concentration (as a thiobarbituric acid adduct by high-performance liquid chromatography) was measured in 56 young IDDM patients and in a group of 32 age-, sex-, BMI-, and **smoking** habit-matched healthy subjects. RESULTS: Plasma **MDA** concentration in IDDM patients was significantly higher than that in healthy control subjects (mean +/- SE: 0.95 +/- 0.03 vs. 0.54 +/- 0.03 mumol/l; P < 0.0001). After stratification by **smoking** status, it was seen that diabetic smokers had values of age, BMI, serum lipids, blood pressure, metabolic control, and diabetes duration and its chronic complications superimposable on those of their non**smoking** counterparts. Nevertheless, plasma MDA concentration was significantly higher in IDDM patients who smoked than in IDDM patients who didn't smoke (1.03 +/- 0.4 vs. 0.87 +/- 0.03 mumol/l; P = 0.002), without any sex difference with regard to MDA levels. CONCLUSIONS: These data show an increase in circulating products of lipid peroxidation in young diabetic smokers, thus further supporting the clinical importance of discouraging the initiation of **smoking** as well as promoting its cessation in people with IDDM.

PM3000457366

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70: J Investig Allergol Clin Immunol 1996 Sep-Oct;6(5):294-300

Modification of human LDL by in vitro incubation with cigarette smoke or copper ions: implications for allergies, asthma and atherosclerosis.

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Division of Clinical Nutrition and Metabolism, University of California, Davis, USA.

Cigarette **smoking** has been linked to a higher risk of not only atherosclerosis and related diseases, but asthma and allergies as well. The mechanisms linking **smoking** to these diseases may be due in part to increased low density lipoprotein (**LDL**) modification. In the current study, we compared the modification in vitro of **LDL** isolated from healthy volunteers that had been exposed to either the gas phase of cigarette smoke or copper ion mediated oxidation. The study used as measures of modification/damage the levels of protein carbonyl groups, changes in electrophoretic mobility on agarose gel electrophoresis and levels of thiobarbituric-reacting substances. Other measures used to assess other aspects of **LDL** modification included SDS PAGE and immunoblotting. Both copper ion or exposure to the gas phase of cigarette smoke increased electrophoretic mobility of **LDL** but the increase was greater in the gas phase smoke group. In contrast, thiobarbituric reacting substance levels were increased primarily in copper oxidized **LDL**. Protein carbonyl levels were increased to a similar extent in both copper ion and smoke exposed samples. Addition of EDTA prevented the modifications found upon copper mediated oxidation of **LDL**, but EDTA did not prevent the modification of the gas phase cigarette smoke exposed **LDL**. In summary, the results indicate that protein carbonyl formation can be used as a measure of the modification of **LDL** particles and, using several different assessment techniques, there are distinct differences in the modified **LDL** produced by in vitro incubation with gas phase cigarette smoke relative to that found upon incubation of **LDL** with copper ion. The in vitro **smoking**-produced **LDL** modifications may potentially be relevant to the process of lipoprotein modification in vivo and to the subsequent biological effects of these modified lipoproteins on processes affected by the immune system involvement, such as atherosclerosis and allergy/asthma.

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71: Circulation 1996 Aug 15;94(4):614-21

Effects of cigarette smoking on the angiographic evolution of coronary atherosclerosis. A Canadian Coronary Atherosclerosis Intervention Trial (CCAIT) Substudy. CCAIT Study Group.

Waters D, Lesperance J, Gladstone P, Boccuzzi SJ, Cook T, Hudgin R, Krip G, Higginson L

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BACKGROUND: Although **smoking** increases both the risk of developing coronary disease and the risk of coronary events in patients with known coronary atherosclerosis, the effect of **smoking** on the evolution of coronary atherosclerosis as assessed by serial angiography is poorly defined. METHODS AND RESULTS: Ninety smokers with coronary atherosclerosis shown on a recent angiogram and with fasting cholesterol levels between 220 and 300 mg/dL were enrolled in a randomized, double-blind, placebo-controlled trial of cholesterol-lowering therapy, along with 241 nonsmokers and exsmokers. Lovastatin at a mean dose of 36 mg/d lowered total and **LDL** cholesterol by 21 +/- 11% and 29 +/- 11%, respectively, but these levels changed by < 2% in placebo-treated patients. Coronary arteriography was repeated after 2 years in 72 smokers and their 557 lesions were measured blindly with an automated quantitative system, along with 1752 lesions in 227 nonsmokers. Coronary change score, the per-patient mean of the minimal lumen diameter changes for all qualifying lesions, worsened by 0.16 +/- 0.16 mm in smokers and by 0.07 +/- 0.15 mm in nonsmokers in the placebo group (P < .001). Lovastatin-treated smokers had less worsening (0.07 +/- 0.15 mm) than placebo-treated smokers (P = .024). One or more coronary lesions progressed in 16 of 34 lovastatin-treated smokers and in 28 of 38 placebo-treated smokers (47% versus 74%, P < .001). In the placebo group, new coronary lesions developed in 21 of 38 smokers and in 28 of 115 nonsmokers (55% versus 24%, P < .001); fewer lovastatin-treated smokers developed new lesions (15% versus 55%, P < .001). CONCLUSIONS: **Smoking** accelerates coronary progression and new lesion formation as assessed by serial quantitative coronary arteriography. Lovastatin slows the progression of coronary atherosclerosis and prevents the development of new coronary lesions in smokers.

Publication Types:
Clinical trial
Multicenter study
Randomized controlled trial

Comments:
Comment in: Circulation 1996 Aug 15;94(4):596-8

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

72: Circulation 1996 Jul 1;94(1):19-25

Modulation of oxidant stress in vivo in chronic cigarette smokers.

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BACKGROUND: Free radical-induced oxidative damage is thought to be involved in the pathogenesis of diseases associated with cigarette **smoking**. We examined the production of 8-epi-prostaglandin (PG) F2 alpha, a stable product of lipid peroxidation in vivo, and its modulation by aspirin and antioxidant vitamins in chronic cigarette smokers. METHODS AND RESULTS: We performed the following studies: (1) a cross-sectional comparison of smokers and control subjects, (2) an examination of the dose-response relationship, (3) an exploration of the effect of **smoking** cessation (3 weeks) and nicotine patch supplementation, (4) the effect of aspirin consumption, and (5) the effects of 5 days' dosing with vitamin E (100 and 800 U), vitamin C (2 g), and their combination. 8-epi-**PGF2** alpha excretion (in pmol/mmol, mean +/- SEM) was 176.5+/-30.6 in heavy smokers, 92.7+/-4.8 (P<.05) in moderate smokers, and 54.1+/-2.7 (P<.005) in nonsmokers. Urinary levels fell from 145.5+/-24.9 to 114.6+/-27.1 (week 2, P<.05) and 112.6+/-24.9 (week 3, P<.05) on cessation of **smoking**. Aspirin treatment failed to suppress urinary levels of 8-epi-**PGF2** alpha despite a significant reduction in urinary 11-dehydro-**TxB2** production and suppression of 8-epi-**PGF2** alpha and **TxB2** in serum. Vitamin C (pre, 194.6+/-40.9; post, 137.2+/-34.1; P<.05) and a combination of vitamin C and E (pre, 171.0+/-39.8; post, 133.5+/-29.6 P<.05) suppressed urinary 8-epi-**PGF2** alpha, whereas vitamin E alone had no effect. CONCLUSIONS: Urinary 8-epi-**PGF2** alpha may represent a noninvasive, quantitative index of oxidant stress in vivo. Elevated levels of 8-epi-**PGF2** alpha in smokers may be modulated by quitting cigarettes and switching to nicotine patches or by antioxidant vitamin therapy.

Publication Types:
Clinical trial
Randomized controlled trial

PM3000457369

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

73: Atherosclerosis 1996 Jul;124(1):75-81

Increased levels of autoantibodies to cardiolipin and oxidised low density lipoprotein are inversely associated with plasma vitamin C status in cigarette smokers.

Fickl H, Van Antwerpen VL, Richards GA, Van der Westhuyzen DR, Davies N, Van der Walt R, Van der Merwe CA, Anderson R

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In this study we have measured circulating levels of autoantibodies to cardiolipin and oxidised low-density lipoprotein (ox-**LDL**) and correlated these with plasma concentrations of the anti-oxidant nutrients vitamin C, vitamin E and beta-carotene, in a group (79) of asymptomatic, male cigarette smokers and in non-**smoking** control subjects. Cigarette **smoking**, a well-known risk factor for development of atherosclerosis, was found to be associated with moderately elevated levels of autoantibodies to both cardiolipin and ox-**LDL**. Increased levels of these autoantibodies were most evident in the older smokers (> 30 years) and were significantly and inversely correlated with plasma vitamin C, but not with vitamin E or beta-carotene. Absorption studies designed to investigate the specificity of these autoantibodies demonstrated a high degree of cross-reactivity of cardiolipin antibodies with ox-**LDL**, while antibodies to the oxidatively modified lipoprotein tended to be specific for this antigen. These findings suggest that cigarette **smoking** promotes formation of autoantibodies to both cardiolipin and ox-**LDL** and that these may be involved in the initiation and/or perpetuation of atherosclerosis. Dietary intake of vitamin C may be a determinant of susceptibility to development of this cardiovascular disorder.

74: Ann N Y Acad Sci 1996 Jun 15;786:245-51

Modification of high- and low-density lipoproteins by cigarette smoke oxidants.

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PM3000457370

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

75: J Cardiovasc Risk 1996 Jun;3(3):307-11

Inter-relationships of plasma fibrinogen, low-density lipoprotein cholesterol, cigarette smoking and the prevalence of cardiovascular disease.

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BACKGROUND: The magnitude of the cardiovascular risk associated with plasma **fibrinogen** concentration is influenced separately by cigarette **smoking** and by low-density lipoprotein (**LDL**) cholesterol levels. The effects of combinations of these factors on risk and the extent to which inclusion of the plasma **fibrinogen** level further refines the risks associated with **smoking** and high **LDL** cholesterol levels are not known. OBJECTIVE: To determine the inter-relationships among all of the three factors **smoking**, **LDL** cholesterol level and **fibrinogen** level with respect to the occurrence of cardiovascular disease. METHODS: The study was part of the Edinburgh Artery Study, which was a cross-sectional random sample survey of 1592 men and women aged 55-74 years. The assessment of cardiovascular disease included recall of diagnosis by a doctor of angina or myocardial infarction, intermittent claudication determined by a questionnaire and measurement of ankle systolic blood pressure. RESULTS: The odds ratio for disease in smokers in the top tertiles of plasma **fibrinogen** and **LDL** cholesterol levels was 7.7 (95% confidence interval 3.0-19.8; P < or = 0.001). Neither a multiplicative nor a synergistic effect of the three factors on the odds of disease was observed but the level of each contributed to the risk. For example, in current smokers in the bottom tertile of **LDL** cholesterol level, the odds of disease were 6.1 (95% confidence interval 2.2-17.0; P < or = 0.001) in the top tertile, 2.9 (95% confidence interval 1.0-8.6; P < or = 0.05) in the middle tertile and 1.6 (95% confidence interval 0.5-4.8; P > 0.05) in the bottom tertile of plasma **fibrinogen** level. Subjects in the bottom tertile of plasma **fibrinogen** level did not have significantly elevated (P < 0.05) risks irrespective of **LDL** cholesterol levels and **smoking** status. CONCLUSION: The incorporation of plasma **fibrinogen** level permitted more precise delineation of the odds of disease within categories of **smoking** and **LDL** cholesterol concentration. These relationships need to be investigated further in prospective studies.

PM3000457371

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76: Cardiovasc Res 1996 Jun;31(6):975-83

Enhanced modifications of low-density lipoproteins (LDL) by endothelial cells from smokers: a possible mechanism of smoking-related atherosclerosis.

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OBJECTIVE: The aim of the study was to investigate **LDL** modifications by cultured human umbilical vein endothelial cells (HUVEC) from women smokers and non-smokers. METHODS: Modifications of **LDL** by HUVEC were studied by determining the values of **thiobarbituric acid-reactive substances** (**TBARS**) and the percentage of the most electronegative oxidized **LDL** fraction (fraction C) by using an ion-exchange chromatographic method based on fast protein liquid chromatography (FPLC). We also studied the cellular production of superoxide anion, the effect of various inhibitors and cysteine, and determined total intracellular glutathione content and cell growth. RESULTS: **LDL** exposed to HUVEC from smokers for 48 h showed significantly greater modifications than **LDL** exposed to HUVEC from non-smokers, as assessed by **TBARS** determination (19.4 +/- 1.2, mean +/- s.e.m., n = 20 versus 15.4 +/- 0.7 nmol/mg **LDL**, n = 19; P < 0.01) and by FPLC (percentage of fraction C: 39 +/- 7, n = 29 versus 14 +/- 3, n = 34; P < 0.001). Moreover, HUVEC from smokers produced significantly more superoxide anion than those from non-smokers (0.46 +/- 0.13 nmol/10(5) cell/min, n = 9 versus 0.22 +/- 0.05, n = 10; P < 0.05). Superoxide production, like cell-induced modification of **LDL**, was strongly dependent on the presence of cysteine in the medium. Furthermore, HUVEC from smokers had a significantly (P < 0.05) higher total intracellular glutathione content than those from non-smokers (39.9 +/- 3.1 nmol/mg, n = 9 versus 31.8 +/- 2.2, n = 7). Finally, HUVEC from smokers and non-smokers showed similar growth at 48 h. CONCLUSION: HUVEC from smokers converted significantly more **LDL** into an atherogenic form than HUVEC from non-smokers, a phenomenon that was not due to altered cell growth. HUVEC-mediated **LDL** modifications were strongly thiol-dependent, as both **LDL** modifications and superoxide anion production were inhibited in cysteine-free medium. Stimulation of cystine uptake by HUVEC, reflected by the enhanced total glutathione content, could account for the enhanced superoxide anion production. All these observations may be relevant to the pathophysiology of **smoking**-related cardiovascular disease.

PM3000457372

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

77: Int J Food Sci Nutr 1996 May;47(3):227-31
Serum antioxidant potential, and lipoprotein oxidation in female smokers following vitamin C supplementation.

Mulholland CW, Strain JJ, Trinick TR

Health and Health Care Research Unit, School of Clinical Medicine, Queens University, Royal Victorial Hospital, Belfast, UK.

A single blind placebo controlled trial was carried out to assess the effect of high dose vitamin C supplementation on the antioxidant potential, and extent of lipoprotein oxidation of serum in female smokers. Sixteen apparently healthy subjects were randomised into two groups of eight. One group received 1 g of vitamin C for 14 days the other group received a placebo for 14 days. Serum antioxidant potential (TRAP) was measured and lipoprotein oxidation was assessed by measuring serum **malondialdehyde** like material. Despite significant increases in serum C concentrations in the supplemented group, serum TRAP values did not change significantly over the course of the trial. Serum **malondialdehyde** like material also failed to show any temporal variation.
Clinical trial

78: Clin Exp Pharmacol Physiol 1996 May;23(5):397-402
Relationship of cigarette smoking to blood pressure and serum lipids and lipoproteins in men.

Imamura H, Tanaka K, Hirae C, Futagami T, Yoshimura Y, Uchida K, Tanaka A, Laboratory of Nutrition and Exercise Physiology, Nakamura Gakuen University, Fukuoka, Japan.

1. The relationship of cigarette **smoking** to blood pressure and serum lipids and lipoproteins was studied in 7608 men, ranging from 40 to 59 years of age. Analyses were performed separately for non-drinkers and drinkers. 2. After adjusting age and body mass index (BMI) in non-drinkers and age, BMI and alcohol intake in drinkers in forward stepwise multiple regression analysis, there was a dose-dependent negative relationship between cigarette **smoking** and diastolic blood pressure (DBP) and high density lipoprotein cholesterol (**HDL**-C), regardless of drinking habit. There was a dose-dependent positive relationship between cigarette **smoking** and the ratio of total cholesterol (TC) to **HDL**-C (TC:**HDL**-C) in non-drinkers, but not in drinkers. There was a dose-dependent negative relationship between cigarette **smoking** and TC and a positive relationship between cigarette **smoking** and triglycerides (TG) in drinkers, but not in non-drinkers. 3. After matching age and BMI in non-drinkers, subjects who smoked more than 30 cigarettes/day had significantly lower mean values of systolic blood pressure (SBP; 4.3%; $P < 0.05$), DBP (3.0%; $P < 0.01$) and **HDL**-C (15.5%; $P < 0.01$) and higher mean values of TC:**HDL**-C (25.0%; $P < 0.01$), TG (46.8%; $P < 0.01$) and beta-lipoprotein (12.0%; $P < 0.01$) than non-smokers. In drinkers, after matching age, BMI, and alcohol intake, subjects who smoked more than 30 cigarettes/day had significantly lower mean values of SBP (2.8%; $P < 0.05$), DBP (4.8%; $P < 0.01$), **HDL**-C (17.3%; $P < 0.01$) and TC (4.4%; $P < 0.01$) and higher mean values of TC:**HDL**-C (15.4%; $P < 0.01$) and TG (45.1%; $P < 0.01$) than non-smokers. 4. Although the results are somewhat variable, the present study reveals that cigarette **smoking** is negatively associated with SBP and DBP and unfavourably associated with lipids and lipoproteins, regardless of drinking habit.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

79: Gen Pharmacol 1996 Apr;27(3):477-81

Cigarette smoke-modified low density lipoprotein impairs endothelium-dependent relaxation in isolated rabbit arteries.

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1. We investigated the effects of cigarette smoke-modified low-density lipoprotein (CS-**LDL**) on endothelium-dependent relaxations in various isolated rabbit arteries, and compared them with those of oxidized **LDL** (Ox-**LDL**). 2. In aorta rings, acetylcholine-induced endothelium-dependent relaxations were attenuated by preincubation with CS-**LDL** and Ox-**LDL**. Endothelium-independent relaxations induced by sodium nitroprusside were not modified. Similar changes were observed in rings of coronary and basilar arteries. 3. These findings indicate that CS-**LDL**, as well as Ox-**LDL**, may decrease the release or activity of endothelium-derived relaxing factor in vascular endothelial cells.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

80: Circulation 1996 Apr 1;93(7):1346-53

Cigarette smoking potentiates endothelial dysfunction of forearm resistance vessels in patients with hypercholesterolemia. Role of oxidized LDL.

Heitzer T, Yla-Herttuala S, Luoma J, Kurz S, Munzel T, Just H, Olschewski M, Drexler H

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BACKGROUND: Risk factors for atherosclerosis such as hypercholesterolemia and hypertension are associated with endothelial dysfunction of conduit and resistance vessels; however, the interaction of these risk factors and underlying mechanisms affecting endothelial function remain to be determined. The present study investigated the role of long-term **smoking** and hypercholesterolemia and their impact on endothelial function of peripheral resistance vessels in relation to plasma levels of autoantibodies against oxidized **LDL**, which has been implicated in the development of endothelial dysfunction and atherosclerosis. METHODS AND RESULTS: The vascular responses to the endothelium-dependent agent acetylcholine (7.5, 15, 30, and 60 micrograms/min) and the endothelium-independent agent sodium nitroprusside (1,3, and 10 micrograms/min) were studied in normal control subjects (n = 10), patients with hypercholesterolemia (n = 15), long-term smokers (n = 15), and hypercholesterolemic patients who smoked (n = 15). Drugs were infused into the brachial artery, and forearm blood flow (FBF) was measured by venous occlusion plethysmography. The FBF responses to acetylcholine were significantly blunted in all three patient groups compared with normal control subjects ($P < .05$). The acetylcholine-induced increase in FBF was significantly attenuated in patients with hypercholesterolemia who smoked compared with hypercholesterolemic nonsmokers and normocholesterolemic smokers ($P < .05$ for both). The response to sodium nitroprusside was not statistically different in all four groups. Plasma levels of autoantibody titer against oxidized **LDL** were inversely related to acetylcholine-induced changes in FBF ($r = -.53$, $P < .002$) and were substantially increased in the group with both risk factors. CONCLUSIONS: These results demonstrate that cigarette **smoking** and hypercholesterolemia synergistically impair endothelial function and that their combined presence is associated with increased plasma levels of autoantibodies against oxidized **LDL**. These observations raise the possibility that long-term **smoking** potentiates endothelial dysfunction in hypercholesterolemic patients by enhancing the oxidation of **LDL**.

PM3000457375

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

81: Stroke 1996 Apr;27(4):645-9

Cigarette smoking is correlated with the periventricular hyperintensity grade of brain magnetic resonance imaging.

Fukuda H, Kitani M

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BACKGROUND AND PURPOSE: A new studies have observed a significant inverse correlation between cigarette **smoking** or lipid abnormalities and periventricular hyperintensities (PVHs) on T2-weighted magnetic resonance imaging (MRI) scans of the brain, which is surprising because **smoking** and hyperlipidemia are considered risk factors for cerebrovascular disease. We investigated the relation between **smoking** and lipid abnormalities and PVHs on T2-weighted MRIs. METHODS: MRI scans were performed in 253 patients over the age of 40 years, and PVHs were assessed retrospectively by use of a five-point scale. Patients who were receiving medical treatment for hyperlipidemia were excluded. Serum levels of total cholesterol, high-density lipoprotein (**HDL**) cholesterol, and triglycerides were determined in the fasting state by an automated enzymatic procedure. The low-density lipoprotein (**LDL**) cholesterol level was calculated by use of Friedewald's equation. Age, sex, hypertensive status, antihypertensive treatment, presence or absence of diabetes mellitus, and history of stroke were included in the analysis. RESULTS: Multiple linear regression analysis showed that age, hypertension, **smoking**, and antihypertensive treatment were significantly and independently correlated with the PVH score. The standard partial regression coefficients were .39 (P<.0001) for age, .33 (P<.0001) for hypertension, .16 (P=.0062) for **smoking**, and -.18 (P=.0124) for antihypertensive treatment. Hypercholesterolemia (total cholesterol level >220 mg/dL), **HDL** hypocholesterolemia (**HDL** cholesterol level <40 mg/dL, **LDL** hypercholesterolemia (**LDL** cholesterol level > 130 mg/dL), hypertriglyceridemia (triglyceride level >150 mg/dL), sex, diabetes mellitus, and a history of stroke were not correlated with the PVH score. CONCLUSIONS: Cigarette **smoking** was a weak but significant positive predictor of the PVH score and was independent of age, hypertension, and antihypertensive treatment. Lipid abnormalities were not related to the PVH score.

PM3000457376

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

82: Clin Chem 1996 Apr;42(4):524-30

Low-density lipoprotein susceptibility to in vitro oxidation in healthy smokers and nonsmokers.

Siekmeier R, Wulfroth P, Wieland H, Gross W, Marz W

Gustav Embden-Center of Biological Chemistry, J.W. Goethe-University, Frankfurt am Main, Germany.

We analyzed the susceptibility of low-density lipoproteins (**LDL**) to oxidation in 17 healthy smokers (43.3 +/- 16.8 pack-years) and 19 healthy nonsmokers, matched for age (smokers: 52 +/- 7 years; nonsmokers: 53 +/- 7 years), gender, and relative body mass. Cholesterol, triglycerides, **LDL** cholesterol, **HDL** cholesterol, and apolipoprotein (apo) B were not different between smokers and nonsmokers; apo A-I was slightly lower in smokers (one-tailed P = 0.066). To study whether **LDL** from smokers were prone to in vitro oxidation than **LDL** from nonsmokers, we measured the time kinetics of diene formation and the production of **malondialdehyde** during oxidation of **LDL** in vitro. In smokers and nonsmokers, respectively, the mean (+/-SD) lag times (tinh) of diene formation were 111 +/- 26 and 100 +/- 27 min, the peak rates of diene formation (Vmax) were 5.99 +/- 2.34 and 6.34 +/- 2.30 mmol x min-1 x g-1, and the amounts of dienes produced during the propagation phase (dmax) were 250 +/- 264 and 248 +/- 56 mmol x g-1. Neither the **malondialdehyde** content of **LDL** (measured as thiobarbituric acid-reactive substances) before oxidation nor the amount of **malondialdehyde** generated during oxidation (smokers: 57.0 +/- 14.2 micromol x g-1; nonsmokers: 63.2 +/- 15.2 micromol x g-1 indicated any statistically significant effect of **smoking**. When nonsmokers and smokers were considered together, the amount of **malondialdehyde** generated during oxidation correlated with age (nonparametric rs = 0.405), body mass index (r2 = 0.573), and concentrations of apo B (rs = 0.480), cholesterol (rs = 0.448), triglycerides (rs = 0.436), and **LDL** cholesterol (rs = 0.398). Our data show that **smoking** is not associated with increased oxidizability of **LDL** in healthy men and women at ages 42-63 years.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

83: Ann Clin Biochem 1996 Mar;33 (Pt 2):99-106

The effects of cigarette smoking and alcohol consumption on blood lipids: a dose-related study on men.

Whitehead TP, Robinson D, Allaway SL

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The separate and joint effects of cigarette **smoking** and alcohol consumption on serum concentrations of total cholesterol, high-density lipoprotein cholesterol (**HDL**-C), low-density lipoprotein cholesterol (**LDL**-C) and triglycerides were investigated in 46 750 men attending the BUPA Health Screening Centre in London during the period 1983-1987, after allowing for differences in age, body mass index and exercise level. Drinking alcohol was found to raise both total cholesterol and **HDL**-C concentrations, in such a way that **HDL**-C as a percentage of total cholesterol increased with increasing alcohol consumption. **LDL**-C concentrations increased with increasing alcohol consumption in non-smokers, but decreased in those **smoking** over 10 cigarettes per day. Drinking had no significant effect on triglycerides except at high levels of consumption. **Smoking** raised total cholesterol, **LDL**-C and triglycerides, but lowered **HDL**-C concentrations. In particular, **smoking** even small amounts could negate any protective benefit in **HDL**-C concentrations gained from moderate consumption of alcohol. Assuming a desirable lipid profile to consist of low total cholesterol, **LDL**-C and triglycerides and a high **HDL**-C value, this is best achieved for men by being a non-**smoking** moderate drinker.

84: Atherosclerosis 1996 Mar;121(1):23-33

Evidence for more extensive deposits of epitopes of oxidized low density lipoprotein in aortas of young people with elevated serum thiocyanate levels. PDAY Research Group.

Scanlon CE, Berger B, Malcom G, Wissler RW

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Elevated levels of low density lipoprotein (**LDL**) and **smoking** have long been recognized as risk factors for atherosclerosis and coronary heart disease (CHD). However, the mechanisms by which these factors contribute to the disease have not been fully elucidated. It has been postulated from in vitro studies using serum and **LDL** from smokers that **smoking** increases the oxidation of **LDL**, which in turn contributes to atherogenesis. We know of no direct evidence linking oxidized **LDL** (ox**LDL**) in human arteries to increased atherosclerosis in individuals who show elevated serum thiocyanate levels (HST) as an indicator of recent **smoking**. We have studied arterial samples from smokers micromorphometrically and found that 'smokers' have a greater area in which ox**LDL** can be identified in the early stages of the disease than do "nonsmokers', i.e., individuals with low serum thiocyanate levels (LST). This study demonstrates a positive correlation between the extent of ox**LDL** in the fatty streaks as well as the fatty plaques of standardized core sample areas of the thoracic and abdominal aortas of a sample group of young people, aged 15-34, who have evidence of recent **smoking** based on their postmortem serum thiocyanate levels.

PM3000457378

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

85: Diabetes Care 1996 Feb;19(2):112-8

Acute effect of cigarette smoking on glucose tolerance and other cardiovascular risk factors.

Frati AC, Iniestra F, Ariza CR

Department of Internal Medicine, Hospital de Especialidades del Centro Medico La Raza, Mexico City, Mexico.

OBJECTIVE: To investigate the acute effect of cigarette **smoking** on glucose tolerance, insulin sensitivity, serum lipids, blood pressure, and heart rate. RESEARCH DESIGN AND METHODS: This nonrandomized experimental control trial in a tertiary care center included 20 healthy chronic smokers and 20 age-, sex-, and BMI-matched healthy volunteers. Two oral glucose tolerance tests (OGTTs) were performed on each subject. Three cigarettes were smoked during the first 30 min in one of the tests. Serum glucose, insulin, and C-peptide levels were measured every 30 min; the area under the curve (AUC) and the insulin sensitivity index (ISI) were calculated; serum total cholesterol, **LDL** cholesterol, **HDL** cholesterol, and triglyceride levels were measured at 0 and 180 min; and blood pressure and heart rate were recorded every 5 min throughout 180 min. RESULTS: **Smoking** acutely impaired glucose tolerance: the AUC for glucose in smokers was 25.5 +/- 1.03 mmol/l (mean +/- SE) (95% CI 22.9-28) during the **smoking** OGTT and 21.8 +/- 0.85 mmol/l (CI 19.2-24.3) in the control OGTT ($P < 0.01$); in nonsmokers, it was 19.7 +/- 0.3 mmol/l (CI 18.8-20.5) in the **smoking** OGTT and 18.7 +/- 0.35 mmol/l (CI 17.8-19.5) in the control OGTT ($P < 0.05$). **Smoking** acutely increased serum insulin and C-peptide levels and decreased ISI only in smokers: ISI in smokers was 55 +/- 2.8 (CI 47.4-62.6) in the control OGTT and 43 +/- 2.7 (CI 35.4-50.6) in the **smoking** OGTT ($P < 0.05$). **Smoking** acutely caused a rise of serum total cholesterol levels in both groups and increased **LDL** cholesterol and triglyceride serum levels significantly only in smokers ($P < 0.05$). A significant rise of blood pressure and heart rate while **smoking** was present in all the subjects. CONCLUSIONS: **Smoking** acutely impaired glucose tolerance and insulin sensitivity, enhanced serum cholesterol and triglyceride levels, and raised blood pressure and heart rate. These findings support the pathogenetic role of cigarette **smoking** on cardiovascular risk factors.

PM3000457379

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

86: Circulation 1996 Feb 1;93(3):450-6
Smoking, serum lipids, blood pressure, and sex differences in myocardial infarction. A 12-year follow-up of the Finnmark Study.

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BACKGROUND: Few epidemiological studies have investigated the relative importance of major coronary risk factors in the two sexes within the same study population. In particular, it is not clear whether **smoking** carries a similar risk of coronary heart disease in men and women. METHODS AND RESULTS: The associations between **smoking**, serum lipids, blood pressure, and myocardial infarction were examined in a population-based prospective study of 11,843 men and women aged 35 to 52 years at entry. During 12 years, 495 cases of first myocardial infarction among men and 103 cases among women were identified. Myocardial infarction incidence was 4.6 times higher among men. The incidence was increased sixfold in women and threefold in men who smoked at least 20 cigarettes per day compared with never-smokers, and the rate in female heavy smokers exceeded that of never-**smoking** men. Multivariate analysis identified current **smoking** as a stronger risk factor in women (relative risk, 3.3; 95% confidence interval [CI], 2.1 to 5.1) than in men (relative risk, 1.9; 95% CI, 1.6 to 2.3). Among those under 45 years old at entry, the **smoking**-related sex difference was more pronounced (in women: relative risk, 7.1; 95% CI, 2.6 to 19.1) (in men: relative risk, 2.3; 95% CI, 1.6 to 3.2). Serum total cholesterol, **HDL** cholesterol, and systolic blood pressure were also highly significant predictors in both sexes. CONCLUSIONS: **Smoking** was a stronger risk factor for myocardial infarction in middle-aged women than in men. Relative risks associated with serum lipids and blood pressure were similar despite large sex differences in myocardial infarction incidence rates.

PM3000457380

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

87: Atherosclerosis 1996 Jan 26;119(2):139-50

Effect of ascorbate supplementation on low density lipoprotein oxidation in smokers.

Fuller CJ, Grundy SM, Norkus EP, Jialal I

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The oxidative modification of low density lipoprotein (**LDL**) may play a role in the pathogenesis of atherosclerosis. Furthermore, evidence of oxidized **LDL** (ox-**LDL**) has been found in vivo. Supplementation of some animal models with antioxidants has been shown to retard the formation of aortic atherosclerosis. Ascorbate (vitamin C) is a highly potent aqueous-phase antioxidant in plasma, which has been shown in vitro to retard **LDL** oxidation. Cigarette smokers have reduced concentrations of ascorbate in their plasma, and their **LDL** may be more prone to oxidation. Hence, the objective of the present study was to examine the effect of ascorbate depletion and supplementation on the propensity of **LDL** to oxidize in smokers in a 6-week study. Nineteen healthy smokers followed a low ascorbate diet (< or = 30 mg/day) for 2 weeks, then were randomly assigned to receive placebo or 1000 mg ascorbate per day for 4 weeks. Blood was taken at 0 and 4 weeks of supplementation for study of **LDL** oxidative susceptibility. **LDL** was oxidized with 5 mumol/l copper. The ascorbate-supplemented group had significant increases in plasma ascorbate. The placebo group showed no change in the time course of **LDL** oxidation between 0 and 4 weeks. However, the ascorbate-supplemented group has a significant reduction in **LDL** oxidative susceptibility as measured by **thiobarbituric acid-reactive substances** (**TBARS**) and the formation of conjugated dienes. The ascorbate-supplemented group demonstrated significantly increased lag phase and decreased oxidation rate at 4 weeks compared to 0 weeks. No changes were found in the placebo group. The ascorbate-supplemented group showed no biochemical signs consistent with increased body iron stores. Supplementation of otherwise healthy smokers for 4 weeks with 1000 mg ascorbate per day resulted in increased plasma ascorbate and reduced **LDL** oxidative susceptibility.

Publication Types:
Clinical trial
Randomized controlled trial

PM3000457381

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

88: Wien Klin Wochenschr 1996;108(18):589-92
[Single passive smoking exposure induces no measurable oxidation of low density lipoproteins].
[Article in German]

Oguogho A, Kritz H, Sinzinger H

Wilhelm-Auerswald Atheroskleroseforschungsgruppe und Universitatsklinik fur Nuklearmedizin, Wien.

Oxidation of low-density lipoproteins (**LDL**) is well known to increase the atherogenic risk. Active **smoking** has been claimed to be associated with a significant oxidant stress determined by enhanced **LDL** oxidation and isoprostane formation. We assessed the susceptibility of **LDL** to oxidation in 9 healthy non-smokers and 7 smokers before and after three and five hours' exposure to passive **smoking**. Baseline values for the lag time, diene formation, **malondialdehyde** and isoprostanes differed in part significantly. In contrast to the data on active **smoking**, passive exposure to cigarette smoke did not significantly affect any of these parameters, nor diene formation and electrophoretic mobility in smokers and non-smokers alike. These results indicate that a single exposure to passive **smoking** does not induce relevant oxidation of **LDL** in men.

89: Pathobiology 1996;64(3):115-22
Peroxidized low-density lipoprotein with four kinds of hydroperoxidized cholesteryl linoleate estimated in plasma of young heavy smokers.

Kanazawa T, Osanai T, Yin XZ, Yi HZ, Onodera K, Metoki H

Second Department of Internal Medicine, Hirosaki University School of Medicine, Japan.

AIM: To clarify the mechanisms of vascular complications due to heavy **smoking**, it was studied whether hydroperoxidized low-density lipoprotein (HPO-**LDL**) was estimated in plasma of young heavy smokers. METHOD: Plasmas were separated from 15 young male students (HS-M) who smoked more than 30 cigarettes/day over 5 years, and from 10 nonsmoker students (NS-M) too. **LDL** was isolated by ultracentrifugation. HPO-cholesteryl linoleate (HPO-CL) was identified by thin-layer chromatography (TLC), and lipid peroxide was measured by Determiner LPO (Kyowa Medics Co., Ltd, Tokyo, Japan). The molecular structure of lipid peroxide in **LDL** was identified using GMS analysis, HPLC chromatography and 1H-NMR analysis. RESULTS: (1) HPO-CL was clearly observed on the TLC in **LDL** lipids of HS-M but from NS-M it was barely found. (2) Lipid peroxide in **LDL** separated from HS-M consisted of HPO-CL and reduced HPO-CL. CONCLUSION: Peroxidized **LDL** was estimated in plasma with young heavy smokers. Because of injurious reactions in vessels of peroxidized **LDL**, it is considered that heavy **smoking** is one of the risk factors for vascular complications in heavy smokers.

PM3000457382

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

90: Free Radic Biol Med 1996;20(4):619-24
Measurement of urinary 8-Epi-prostaglandin F2alpha, a novel index of lipid peroxidation in vivo, by immunoaffinity extraction/gas chromatography-mass spectrometry. Basal levels in smokers and nonsmokers.

Bachi A, Zuccato E, Baraldi M, Fanelli R, Chiabrando C
Istituto di Ricerche Farmacologiche 'Mario Negri', Milano, Italy.

8-Epi-prostaglandin F2alpha (8-epi-**PGF2**alpha) is an F2-isoprostane recently identified as a marker of free radical-catalyzed lipid peroxidation in vivo and potential mediator of oxidative damage. Currently, **endogenous 8-epi-PGF2alpha** is measured by gas chromatography-mass spectrometry after lengthy sample preparation. We extracted and purified **8-epi-PGF2alpha** in one step from biological samples on immunoaffinity columns prepared with an anti-**8-epi-PGF2alpha** antiserum, raised in our laboratory. Quantitation was done by stable-isotope dilution gas chromatography/negative-ion chemical ionization mass spectrometry, with selected ion recording. Carboxylate anions of the pentafluorobenzyl ester trimethylsilyl ether derivative **of 8-epi-PGF2alpha** and [2H4]**8-epi-PGF2alpha** were monitored (m/z 569 and 573). Basal urinary excretion of **8-epi-PGF2alpha** can be accurately and rapidly measured by this method. Under normal conditions rats (n = 30) excreted 2.18 +/- 0.68 ng/24 h. In healthy non**smoking** young volunteers, urinary excretion **of 8-epi-PGF2alpha**, measured three times on alternate days, was fairly constant (CV 2-10%). Nonsmokers excreted significantly less **8-epi-PGF2alpha** than age-matched smokers (8.08 +/- 2.3 vs. 18.40 +/- 4.77 ng/h/1.73 m2; n = 6; p < 0.005), as reported by others using different methods.

91: Int J Vitam Nutr Res 1996;66(3):203-9
Plasma concentrations of carotenoids and tocopherols in male long-term tobacco chewers, smokers and nonusers.

Driskell JA, Giraud DW, Sun J, Martin HD
Department of Nutritional Science and Dietetics, University of Nebraska-Lincoln 68583-0806, USA.

Plasma carotenoid and tocopherol concentrations of men, aged 25 to 55 years, who were long-term chewers, smokers, or tobacco nonusers were determined. Tobacco users had either chewed (n = 11) or smoked (n = 23) for > 15 years. Nonusers (n = 10) had never smoked > 1 pack or chewed > 34 g. Food energy, mono- and poly-unsaturated and saturated fats, cholesterol, vitamin A, vitamin E, and carotenoid intakes of the three groups were not significantly different. Chewers and smokers reported consuming significantly less cryptoxanthin, found primarily in some fruits, and had significantly lower plasma cryptoxanthin levels than nonusers. Nonusers had significantly higher concentrations of plasma alpha-tocopherol than smokers; whereas those of chewers were intermediate. Nonusers had significantly higher concentrations of plasma gamma-tocopherol and total tocopherols than chewers or smokers. Plasma delta-tocopherol concentrations of the groups were not significantly different. Nonusers had significantly higher levels of beta-carotene than smokers but not chewers. Plasma lutein and lycopene concentrations of all groups were not significantly different. Dietary intakes of total carotenoids and tocopherols of the three groups were not significantly different, yet nonusers had higher plasma concentrations of total and most individual carotenoids and tocopherols than smokers with values for chewers being intermediate.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

92: Atherosclerosis 1995 Nov;118(1):45-51
Published erratum appears in Atherosclerosis 1996 Apr 5;121(2):295

Lipid peroxidation of circulating low density lipoproteins with age, smoking and in peripheral vascular disease.

Sanderson KJ, van Rij AM, Wade CR, Sutherland WH

Department of Surgery, Otago Medical School, Dunedin, New Zealand.

In this study, lipid peroxides in plasma and the low density lipoprotein (**LDL**) fraction and plasma concentrations of vitamin E, lipids and lipoproteins were measured in 22 smokers (mean age 35 years), 26 non-**smoking** patients with peripheral vascular disease (PVD), mean age 66 years), and 23 younger (ages < or = 55 years) and 26 older (ages > 55 years) healthy subjects. Plasma lipid peroxide concentrations in the PVD patients (105.9 +/- 20.6 vs. 91.8 +/- 15.8 ng **malondialdehyde** (MDA)/ml plasma, mean +/- S.D.) and the smokers (94.1 +/- vs. 74.0 +/- 13.9 ng MDA/ml plasma) were significantly elevated compared with levels in the appropriate control subjects and levels were significantly higher in older compared with younger control subjects. Plasma **LDL** lipid peroxides were also significantly raised in patients with PVD and smokers compared with control values (PVD): 37.1 +/- 7.7 vs. 26.3 +/- 4.1 ng MDA/ml plasma; smokers: 30.4 +/- 6.9 vs 24.9 +/- 7.5 ng MDA/ml plasma). The ratio of **LDL** lipid peroxides: **LDL**-cholesterol was significantly higher in the smokers, and plasma cholesterol and **LDL**-cholesterol were significantly higher in patients with PVD compared with other groups of subjects. The ratio of vitamin E: total lipid was not significantly different between the study groups. These data show that lipid peroxide levels in the plasma **LDL** fraction are elevated along with raised circulating levels in patients with PVD and smokers but that **LDL** lipid peroxide concentrations were independent of age in the healthy subjects. Elevated **LDL** lipid peroxide concentrations may may be mainly due to abnormally high **LDL** levels in PVD patients, whereas in smokers, the concentration of lipid peroxides in the **LDL** particles is raised and might render the lipoprotein more atherogenic.

PM3000457384

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

93: Arterioscler Thromb Vasc Biol 1995 Nov;15(11):1793-7
Coffee consumption, alcohol use, and cigarette smoking as determinants of serum total and HDL cholesterol in two Serbian cohorts of the Seven Countries Study.

Jansen DF, Nedeljkovic S, Feskens EJ, Ostojic MC, Grujic MZ, Bloemberg BP, Kromhout D

Department of Chronic Diseases and Environmental Epidemiology, National Institute of Public Health and Environmental Protection, Bilthoven, The Netherlands.

The associations between serum total and **HDL** cholesterol and three lifestyle factors--consumption of Turkish coffee, consumption of alcohol, and cigarette **smoking**--were examined in two Serbian cohorts of the Seven Countries Study. In 1988 and 1989, 319 men from Zrenjanin and Belgrade, 65 to 84 years old and free of myocardial infraction, participated. The men from Zrenjanin were originally working in a large cooperative, and the men from Belgrade were faculty members of the university. **HDL** cholesterol, alcohol consumption, and cigarette **smoking** were significantly higher in Zrenjanin than in Belgrade. Serum total cholesterol levels and coffee consumption were not different. ANCOVA showed that serum total cholesterol levels were 8.2% higher ($P < .05$) in men consuming two small cups of coffee per day compared with abstainers, and this was also seen after adjustment for cigarette **smoking**, age, body mass index, cohort, and alcohol consumption. In men consuming one or more alcoholic drinks per day (more than 10 g/d alcohol), **HDL** cholesterol levels were increased by 0.19 mmol/L (15.4%) compared with men consuming no alcohol ($P < .001$). This association was stronger in the Zrenjanin cohort than in the Belgrade cohort ($P < .05$). **Smoking** was not associated with total cholesterol or with **HDL** cholesterol levels. In Serbian men, boiled Turkish coffee and alcohol consumption are independently associated with serum total and **HDL** cholesterol levels, respectively.

Publication Types:
Clinical trial
Multicenter study

94: N Engl J Med 1995 Oct 19;333(16):1081-2
Alcohol consumption and mortality among women.

Sijbrands EJ, Smelt AH, Westendorp RG

Publication Types:
Comment
Letter

Comments:
Comment on: N Engl J Med 1995 May 11;332(19):1245-50

PM3000457385

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

95: Clin Sci (Colch) 1995 Oct;89(4):333-42
Smoking and plasma lipoprotein metabolism.

Freeman DJ, Packard CJ

Publication Types:
Editorial
Review
Review literature

96: Ned Tijdschr Geneeskd 1995 Sep 2;139(35):1790-3
[The longitudinal development of smoking behavior in men and women between 13 and 27 years and the relationship with biological risk factors for cardiovascular diseases].
[Article in Dutch]

Twisk JW, van Lenthe FJ, Kemper HC, van Mechelen W

Vrije Universiteit, faculteit der Bewegingswetenschappen, vakgroep Gezondheidkunde, Amsterdam.

OBJECTIVE. To describe the longitudinal development of **smoking** behaviour from adolescence (age 13 years) into young adulthood (age 27 years) and to analyse the longitudinal relationship between **smoking** behaviour and biological risk factors for cardiovascular disease. DESIGN. Longitudinal. SETTING. Amsterdam school children. METHODS. This study was carried out as part of the Amsterdam Growth and Health Study, an observational longitudinal study. Six measurements were carried out over a period of 15 years in 84 males and 98 females, and included a questionnaire regarding **smoking** behaviour and blood analysis for cholesterol parameters. Tracking analysis and generalized estimating equations analysis were used. RESULTS. Both the percentage of smokers and the amount of tobacco smoked by smokers increased until the age of 21 years. After that **smoking** behaviour remained more or less stable in males and decreased slightly in females (period effect). Between 16 and 21 years half the number of persons tried to stop **smoking** but failed to succeed. The development of **smoking** behaviour appeared to be related to low systolic blood pressure and to development of a negative risk profile regarding hypercholesterolaemia (i.e. low high-density lipoprotein (**HDL**) cholesterol and high ratio of total cholesterol and **HDL** cholesterol). There was no relationship between **smoking** and the amount of subcutaneous fat.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

97: Jpn Circ J 1995 Aug;59(8):541-6
CETP and LCAT activities are unrelated to smoking and moderate alcohol consumption in healthy normolipidemic men.

Ito T, Nishiwaki M, Ishikawa T, Nakamura H

First Department of Internal Medicine, National Defense Medical College, Tokorozawa, Japan.

To distinguish between the effects of **smoking** and drinking on lipid metabolism, we conducted a cross-sectional study using 52 healthy normolipidemic subjects who either smoked or drank, but not both. The subjects were divided into three groups: Group S, smokers who did not drink (n = 20); Group D, drinkers who did not smoke (n = 12); and Group C, controls (n = 20), who neither drank nor smoked. High density lipoprotein cholesterol (**HDL**-C) levels and plasma cholesteryl ester transfer protein (CETP) and lecithin: cholesterol acyltransferase (LCAT) activities were measured in all of the subjects, and the values obtained in Group S and Group D were compared to those of controls. Group S had lower ($p < 0.01$) **HDL**2-C and **HDL**3-C levels, and Group D had higher ($p < 0.05$) **HDL**2-C and **HDL**3-C levels than the controls, but there were no significant differences between groups with respect to CETP and LCAT activities. Thus, in healthy normolipidemic men, both **smoking** and drinking affect **HDL**-C levels as expected, but do not affect plasma CETP or LCAT activity levels.

98: QJM 1995 Jul;88(7):503-8
Smoking habits and lipoproteins in British women.

Razay G, Heaton KW

University Department of Medicine, Bristol Royal Infirmary, UK.

The incidence of coronary heart disease is increasing in women. Some of this may be related to increased **smoking** in women over the past decades. However, the mechanism mediating the **smoking**-coronary heart disease link is unclear. We therefore assessed the relationship of **smoking** habits to fasting plasma insulin, total and low-density lipoprotein (**LDL**) cholesterol, triglyceride, high-density lipoprotein (**HDL**) cholesterol, including its subfractions **HDL**2 and **HDL**3, body mass index, and waist:hip circumference ratio in 1048 women aged 25-69 years. Compared with non-smokers, current smokers had higher plasma concentrations of **LDL** cholesterol by 0.2 mmol/l or 6%, total/**HDL** cholesterol ratio by 0.5 or 13%, triglyceride by 0.14 mmol/l or 13% and waist:hip ratio by 0.02 or 3%, but lower **HDL** cholesterol by 0.13 mmol/l or 9% and **HDL**2 cholesterol by 0.07 mmol/l or 13%, while ex-smokers had higher waist hip ratio by 0.01 or 1% but lower **HDL** cholesterol by 0.06 mmol/l or 4% and **HDL**2 cholesterol by 0.09 mmol/l or 16%. Ex-smokers for up to 5 years, compared with non-smokers, had higher plasma concentrations of total/**HDL** cholesterol ratio by 0.4 mmol/l or 11%, triglyceride by 0.22 mmol/l or 21% and waist hip ratio by 0.01 or 1%, but lower levels of **HDL** cholesterol by 0.12 mmol/l or 9% and **HDL**2 cholesterol by 0.14 mmol/l or 26%. Cigarette **smoking** is associated with adverse changes in lipoprotein levels; these changes decrease slowly after quitting.

PM3000457387

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

99: J Clin Endocrinol Metab 1995 Jul;80(7):2181-5

Impact of chronic cigarette smoking on body composition and fuel metabolism.

Jensen EX, Fusch C, Jaeger P, Peheim E, Horber FF

Klinik Schloss Mammern, Switzerland.

Cigarette **smoking** has been associated with increased upper body fat deposition, as estimated by the waist to hip ratio, which has been shown to be associated with glucose intolerance and dyslipidemia in non**smoking** subjects. Whether **smoking** is at the origin of central adiposity and its related metabolic disturbances is unclear. Moreover, it is controversial whether **smoking** influences fuel metabolism. Therefore, young healthy male volunteers **smoking** more than 10 cigarettes/day for more than 5 yr (n = 14) were compared with nonsmokers (n = 13) matched for age, sex, body mass index, alcohol consumption, physical activity, as well as family history for hypertension, diabetes, obesity, and coronary heart disease. After an overnight fast, blood was drawn for chemistry, body composition was assessed by dual energy x-ray absorptiometry, and fuel metabolism was determined by indirect calorimetry. Nicotine uptake was estimated by 24-h urinary excretion of cotinine. Lean and fat body mass as well as their respective segmental distribution (i.e. arms, trunk, legs, and head), total bone mineral content, resting energy expenditure, and fat, carbohydrate, and protein oxidation were similar between smokers and nonsmokers. In contrast, 24-h urinary cotinine excretion (72.0 +/- 11.4 vs. 0.8 +/- 0.2 mumol/L.24 h; P < 0.001), plasma glucose (4.62 +/- 0.09 vs. 4.25 +/- 0.1 mmol/L; P < 0.01), total cholesterol (4.87 +/- 0.15 vs. 4.27 +/- 0.16 mmol/L; P < 0.02), low density lipoprotein cholesterol (3.05 +/- 0.19 vs. 2.43 +/- 0.16 mmol/L; P < 0.02), and apolipoprotein B concentrations (1.09 +/- 0.11 vs. 0.83 +/- 0.03 mmol/L; P < 0.03) were all higher in smokers than in nonsmokers. In smokers, 24-h urinary cotinine excretion positively correlated with the waist to hip ratio (r = 0.58; P = 0.03) and negatively with hip circumference (r = 0.87; P < 0.001). Moreover, 24-h cotinine excretion positively correlated with fat oxidation (r = 0.57; P = 0.03), but was independent of the other metabolic parameters studied. These results suggest that the dyslipidemia and glucose intolerance observed in smokers are not related to either central obesity or the amount of nicotine inhaled, but, rather, are due to some other component in cigarette smoke. In contrast, in smokers, fat oxidation increases with increasing nicotine uptake, a fact that might account for the often observed weight gain after cessation of **smoking**, thus suggesting different mechanisms of action of tobacco consumption on cholesterol and glucose metabolism on one side and fat oxidation on the other.

PM3000457388

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

100: J Occup Environ Med 1995 Jul;37(7):856-61
Published erratum appears in J Occup Environ Med 1995 Sep;37(9):1121
High-density lipoprotein-cholesterol: determining hygienic factors for intervention.

Anzalone DA, Anzalone FL, Fos PJ

HRS Monroe County Public Health Unit, Naval Medical Clinic of the United States Navy.

Current guidelines of the Adult Treatment Panel on High-Density Lipoprotein-Cholesterol (**HDL**-C) emphasize the protective effect of **HDL**-C in reducing one's risk for coronary heart disease and recommend that individuals with serum **HDL**-C levels below 35 mg/dL utilize hygienic means to raise them. A cross-sectional study was performed to examine the relationship of the hygienic factors obesity (measured by percent body fat and body mass index), **smoking**, and aerobic exercise to **HDL**-C. The sample, consisting of 1701 male employees of a large aerospace hardware assembly plant, were evaluated by health risk appraisal and anthropometric measurement. Regression analysis revealed a significant negative relationship between body mass index, percent body fat, age, **smoking** and the level of **HDL**-C in the blood. Alcohol consumption was directly related to **HDL**-C, and Whites had a lower **HDL**-C than all other races combined. Aerobic exercise was not found to be significantly related to **HDL**-C. A model (multiple R2 = .1136) consisting of age, race, alcohol consumption, **smoking**, and body mass index fit the data well. These findings justify weight management and **smoking** cessation interventions for raising **HDL**-C. However, the role of aerobic exercise was not supported in this study as a means of raising **HDL**-C. Future studies should use maximum oxygen consumption as a measure of aerobic capacity, which may be a better indicator of aerobic exercise level. The role of medication and genetic and dietary factors in **HDL**-C management should also be explored. Although findings from this study support **smoking** cessation and weight management interventions, longitudinal research is needed to determine the most effective strategy for **HDL**-C management.

Publication Types:
Review
Review literature

PM3000457389

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

101: J Am Diet Assoc 1995 Jun;95(6):671-5

Dietary supplementation with orange and carrot juice in cigarette smokers lowers oxidation products in copper-oxidized low-density lipoproteins.

Abbey M, Noakes M, Nestel PJ

Division of Human Nutrition, Commonwealth Scientific and Industrial Research Organization, Adelaide, Australia.

OBJECTIVE: Our objective was to evaluate the effect of daily supplementation with foods high in vitamin C and beta carotene on plasma vitamin levels and oxidation of low-density lipoprotein (**LDL**) in cigarette smokers. SUBJECTS: Fifteen normolipidemic male cigarette smokers who did not usually take vitamin supplements were recruited into the study. INTERVENTIONS: Throughout the study, subjects consumed a diet rich in polyunsaturated fatty acids, which provided 36% of energy as fat: 18% from meat, dairy products, vegetable oils, and fat spreads and 18% from walnuts (68 g/day). Subjects consumed a vitamin-free drink daily for 3 weeks; then for 3 weeks they consumed daily supplements of orange juice (145 mg vitamin C) and carrot juice (16 mg beta carotene). RESULTS: Vitamin-rich food supplements raised plasma levels of ascorbic acid (1.6-fold; P < .01) and beta carotene (2.6-fold; P < .01). **Malondialdehyde**, one end product of oxidation, was lower in copper-oxidized **LDL** after vitamin supplementation (mean +/- standard error = 65.7 +/- 2.0 and 57.5 +/- 2.9 mumol/g **LDL** protein before and after supplementation, respectively; P < .01). Rate of **LDL** oxidation and lag time before the onset of **LDL** oxidation were not affected by antioxidant supplementation. CONCLUSIONS: In habitual cigarette smokers, antioxidant vitamins, which can be feasibly provided from food, partly protected **LDL** from oxidation despite a diet rich in polyunsaturated fatty acids.

Publication Types:
Clinical trial

PM3000457390

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

102: N Engl J Med 1995 May 4;332(18):1198-203

Increase in circulating products of lipid peroxidation (F2-isoprostanes) in smokers. Smoking as a cause of oxidative damage.

Morrow JD, Frei B, Longmire AW, Gaziano JM, Lynch SM, Shyr Y, Strauss WE, Oates JA, Roberts LJ 2nd

Department of Medicine, Vanderbilt University, Nashville, TN 37232-6602, USA.

BACKGROUND. It has been hypothesized that the pathogenesis of diseases induced by cigarette **smoking** involves oxidative damage by free radicals. However, definitive evidence that **smoking** causes the oxidative modification of target molecules in vivo is lacking. We conducted a study to determine whether the production of F2-isoprostanes, which are novel products of lipid peroxidation, is enhanced in persons who smoke. METHODS. We measured the levels of free F2-isoprostanes in plasma, the levels of F2-isoprostanes esterified to plasma lipids, and the urinary excretion of metabolites of F2-isoprostanes in 10 smokers and 10 nonsmokers matched for age and sex. The short-term effects of **smoking** (three cigarettes smoked over 30 minutes) and the effects of two weeks of abstinence from **smoking** on levels of F2-isoprostanes in the circulation were also determined in the smokers. RESULTS. Plasma levels of free and esterified F2-isoprostanes were significantly higher in the smokers (242 +/- 147 and 574 +/- 217 pmol per liter, respectively) than in the nonsmokers (103 +/- 19 and 345 +/- 65 pmol per liter; P = 0.02 for free F2-isoprostanes and P = 0.03 for esterified F2-isoprostanes). **Smoking** had no short-term effects on the circulating levels of F2-isoprostanes. However, the levels of free and esterified F2-isoprostanes fell significantly after two weeks of abstinence from **smoking** (250 +/- 156 and 624 +/- 214 pmol per liter, respectively, before the cessation of **smoking**, as compared with 156 +/- 67 and 469 +/- 108 pmol per liter after two weeks' cessation; P = 0.03 for free F2-isoprostanes and P = 0.02 for esterified F2-isoprostanes). CONCLUSIONS. The increased levels of F2-isoprostanes in the circulation of persons who smoke support the hypothesis that **smoking** can cause the oxidative modification of important biologic molecules in vivo.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

103: Clin Cardiol 1995 May;18(5):267-72
High-density lipoprotein cholesterol level and smoking modify the prognosis of patients with coronary vasospasm.

Miwa K, Fujita M, Miyagi Y, Inoue H, Sasayama S

Second Department of Internal Medicine, Toyama Medical and Pharmaceutical University, Japan.

A cardiovascular event analysis was performed in a subset of 80 consecutive patients with vasospastic coronary artery disease. During the follow-up period (30 +/- 2 months, mean +/- SD), 9 patients had vascular accidents, including acute myocardial infarction, unstable angina, and stroke (Group A), while the remaining 71 patients were eventfree (Group B). Serum total-cholesterol, low-density lipoprotein cholesterol, and triglyceride levels were not different between the two groups at the baseline as well as after follow-up. However, the **HDL**-C level at baseline was significantly lower in Group A (33.5 +/- 2.6 mg/dl) than in Group B (41.9 +/- 1.7 mg/dl, p < 0.05). The **HDL**-C level increased significantly during the follow-up in Group B (delta **HDL**-C: 6.2 +/- 1.2 mg/dl, p < 0.01), but not in Group A (delta **HDL**-C: -3.2 +/- 2.7 mg/dl). The **HDL**-C level after follow-up was significantly lower in Group A (30.3 +/- 2.9 mg/dl) than in Group B (48.1 +/- 1.5 mg/dl, p < 0.01). Current smokers at the end of the follow-up period were more prevalent in Group A (67%) than in Group B (11%, p < 0.01). Cardiovascular accidents occurred more often in current smokers (6/14, 43%) at the end of the follow-up than in current nonsmokers, including quitters (3/66, 5%; p < 0.05). The **HDL**-C level was increased significantly (delta **HDL**: 6.2 +/- 1.3 mg/dl, p < 0.01) in the latter patients, but not in the former (delta **HDL**: -0.4 +/- 2.9 mg/dl).(ABSTRACT TRUNCATED AT 250 WORDS)
PMID: 7628132, UI: 95354337

104: J Clin Pathol 1995 Apr;48(4):385-7
Free radical activity in young adult cigarette smokers.

Leonard MB, Lawton K, Watson ID, MacFarlane I

Department of Clinical Chemistry, Fazakerley Hospital, Liverpool.

Cigarette smoke is capable of generating free radicals. In this study markers of free radical activity (thiobarbituric acid reactivity, superoxide dismutase and glutathione peroxidase) were measured in young adult **smoking** and non-**smoking** volunteers. No significant differences were found in any of the free radical markers between the two groups. The number of leucocytes was elevated and a positive correlation was found between the number of leucocytes and thiobarbituric acid reactivity in the smokers. The results from this study suggest that any free radical activity generated from long term cigarette **smoking** in young adults is adequately scavenged.
PMID: 7615864, UI: 95340907

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

105: J Intern Med 1995 Feb;237(2):161-8

Lowering of body iron stores by blood letting and oxidation resistance of serum lipoproteins: a randomized cross-over trial in male smokers.

Salonen JT, Korpela H, Nyyssonen K, Porkkala E, Tuomainen TP, Belcher JD, Jacobs DR Jr, Salonen R

Research Institute of Public Health, University of Kuopio, Finland.

OBJECTIVES. The purpose of this study was to test the hypothesis that the reduction of body iron stores by venesection (blood letting) would reduce the susceptibility to oxidation of atherogenic serum lipoproteins. DESIGN. This is a randomized, controlled cross-over trial in 14 regularly **smoking** men with elevated serum ferritin concentration. The study design comprised two 14-week study periods, with a 14-week wash-out period in between, with either blood donations or control. SETTING. The study site was the Research Institute of Public Health, University of Kuopio. Investigators from the Division of Epidemiology, University of Minnesota, Minneapolis, participated in the planning of the study. SUBJECTS. Fourteen volunteers who were heavy smokers and had previous experience in blood letting were recruited for the study. INTERVENTIONS. During the intervention periods, the subjects donated 450 mg (500 mL) of blood three times in 14 weeks. MAIN OUTCOME MEASUREMENTS. Oxidation resistance of very low density lipoprotein (V**LDL**)/low density lipoprotein (**LDL**) was measured after inducing oxidation with haemin and H2O2. RESULTS. Serum ferritin concentration was reduced by 44% [95% confidence interval (CI) 8-82%, P = 0.021] during the venesection periods, the maximal oxidation velocity was decreased by 20% (95% CI 3-30%, P = 0.032), and the lag time to start of oxidation was lengthened (oxidation resistance increased) by 33% (95% CI 1-64%, P = 0.036). CONCLUSIONS. These observations indicate that the reduction of body iron stores by venesection can increase the oxidation resistance of serum V**LDL**/**LDL** in regularly **smoking** men.

Publication Types:
Clinical trial
Randomized controlled trial

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

106: Clin Auton Res 1995 Feb;5(1):31-6
Smoking induced differences in autonomic responses in military pilot candidates.

Kotamaki M

Wihuri Research Institute, Helsinki, Finland.

The effects of **smoking** on autonomic function, the renin-angiotensin-aldosterone system, plasma catecholamine and 11-dehydro-thromboxane B2 values were studied in 37 young male military pilot candidates, 19 smokers and 18 non-smokers. There was a higher diastolic blood pressure at rest and higher systolic blood pressure after 5 min during the orthostatic test in smokers. Smokers also had higher diastolic blood pressure levels after exercise in the hand-grip test. Smokers had a lower Valsalva ratio and higher tachycardia ratio in the modified Valsalva manoeuvre, suggesting a degree of autonomic dysfunction. Plasma renin levels at rest and plasma noradrenaline levels after hand-grip test were significantly higher in smokers, implying increased sympathetic activity and enhanced activation of the renin-angiotensin system. Our findings indicate that **smoking** in fit young men increases sympathetic activity and changes physiological responses to autonomic tests.
Publication Types:
Clinical trial
Randomized controlled trial

107: Ann N Y Acad Sci 1995 Jan 17;748:294-300
Cigarette smoke and lipoprotein modification. A possible interpretation for development of atherosclerosis.

Yokode M, Nagano Y, Arai H, Ueyama K, Ueda Y, Kita T

Department of Geriatric Medicine, Kyoto University, Japan.

PM3000457394

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

108: J Environ Pathol Toxicol Oncol 1995;14(3-4):181-92

Cigarette smoke increases cholesterol oxidation and lipid peroxidation of human low-density lipoprotein and decreases its binding to the hepatic receptor in vitro.

Mahfouz MM, Hulea SA, Kummerow FA

Burnsides Research Laboratory, University of Illinois, Urbana 61801, USA.

Low-density lipoprotein (**LDL**) was exposed to six puffs of cigarette smoke (CS) filtered through a glass wool filter and then incubated for 6 or 20 h at 37 degrees C. Control **LDL** was similarly treated but exposed to air. In cigarette smoke-treated **LDL** (CS-**LDL**), compositional changes of the lipid fraction were most detectable after 20 h incubation. These changes included a decrease of polyunsaturated fatty acids (PUFA), slight degradation of phosphatidylethanolamine (PE) and phosphatidylcholine (PC) to their lysophospholipid lysoPE and lyso-PC, elevation of oxidized cholesterol content as well as thiobarbituric acid reacting substance (**TBARS**), indicating an oxidative effect of CS on **LDL**. CS-**LDL** also showed higher anodic electrophoretic mobility and crosslinking of its apoprotein by nondisulfide bonds. The binding affinity of CS-**LDL** to liver membrane receptor was much lower than control **LDL** as measured by the calcium-dependent binding of **LDL**-gold conjugate to the solubilized membrane protein dot blotted onto nitrocellulose strips. Our results indicate that CS induces changes in **LDL**, making it more atherogenic and cytotoxic.

109: Women Health 1995;23(4):27-38

The relationship between smoking, cholesterol, and HDL-C levels in adult women.

Jacobson BH, Aldana SG, Adams TB, Quirk M

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The purpose of this study was to determine the independent relationship between **smoking** quantity and cholesterol (TC) and lipoprotein levels (**HDL**-C) in women. A total of 805 female subjects were grouped as: non-smokers, ex-smokers, light smokers, moderate smokers, and heavy smokers. TC and **HDL**-C were examined before and after controlling for the coexisting risk factors of age, body composition, fitness level, dietary fat intake, family history of coronary artery disease, oral contraceptive, and alcohol use. Preliminary analysis demonstrated significant differences ($p < .01$) in TC between heavy smokers and all other groups and significant differences in **HDL**-C between heavy to moderate smokers and ex- and non-smokers. After adjusting for confounding variables, the differences in TC and **HDL**-C remained unchanged between the groups. It was concluded that heavy to moderate **smoking** was independently associated with higher TC and lower **HDL**-C levels, and that **smoking** abstinence or **smoking** cessation may be associated with healthier lipoprotein profiles in adult women. Based on these findings, it was recommended that employers consider the provision of health promotion programs including seminars, behavioral modification workshops, as well as financial incentives for employees to stop **smoking**.

PM3000457395

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

110: Genet Epidemiol 1995;12(5):499-508
Apolipoprotein B gene DNA polymorphisms (EcoRI and MspI) and serum lipid levels in the Serbian healthy population: interaction of rare alleles and smoking and cholesterol levels.

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Laboratory for Radiobiology and Molecular Genetics, VINCA Institute of Nuclear Sciences, Belgrade, Yugoslavia, Serbia.

The frequency of restriction fragment length polymorphisms (RFLPs) of the apolipoprotein B (apo B) gene, detected by EcoRI and MspI, and their influence on serum lipids were studied in a total of 239 healthy subjects from the Belgrade area. The influence of interaction between different genotypes and **smoking** was also studied. The relative frequency of both rare R2 and M2 alleles (lacking the cutting site) was similar to that reported in other groups of Caucasians (0.16 and 0.11, respectively). No association was observed between the apo B genotypes and serum lipid levels adjusted for age, body mass index, and blood pressure either in the whole sample or in either women or men. When smokers and non-smokers were considered separately, **smoking** had a significant impact on total cholesterol variability in all individuals with genotype M1M2 and high density lipoprotein (**HDL**) cholesterol variability in women with genotype R1R2. The presence of the rare alleles of these two polymorphisms in smokers was associated with lower lipid levels in the whole sample and in both women and men analyzed separately, except for an increase of **HDL** cholesterol level in male smokers, heterozygous for EcoRI polymorphism (R1R2).

111: Diabet Med 1995 Jan;12(1):46-50
Cigarette smoking and free radical activity in young adults with insulin-dependent diabetes.

Leonard MB, Lawton K, Watson ID, Patrick A, Walker A, MacFarlane I

Department of Clinical Chemistry, Fazakerley Hospital, Liverpool, UK.

Cigarette smoke is potentially capable of generating a high free radical load in the body and many patients with diabetes are smokers. This study was designed to investigate the relationship between long-term **smoking** and free radical activity in young adult insulin-dependent diabetic patients with no evidence of macrovascular disease. Eight-five patients (48 male) aged 17-40 years were studied. Mean duration of diabetes was 10.5 years (0.08-33) and 39 were cigarette smokers. All had normal serum creatinine levels. The free radical markers measured were: thiobarbituric acid reactive substances, glutathione peroxidase, and superoxide dismutase. No significant differences in thiobarbituric acid reactive substances, glutathione peroxidase, or superoxide dismutase, were found between the diabetic smokers and non-smokers. Also no difference was found comparing the diabetic patients with 40 non-diabetic control subjects (20 smokers). Persistent albuminuria was present in 16 patients (10 microalbuminuria) and free radical marker concentrations in these subjects were similar to the normoalbuminuric patients. This data suggests that any increase in free radical activity due to cigarette smoke is adequately scavenged in young adults with diabetes who are free of significant macrovascular disease.

PM3000457396

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

112: Arterioscler Thromb 1994 Oct;14(10):1581-5

Higher plasma lipid transfer protein activities and unfavorable lipoprotein changes in cigarette-smoking men.

Dullaart RP, Hoogenberg K, Dikkeschei BD, van Tol A

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The mechanism responsible for the atherogenic lipoprotein changes associated with cigarette **smoking** are largely unknown. Lecithin: cholesterol acyltransferase (LCAT) and cholesteryl ester transfer protein (CETP) are key factors in the esterification of plasma cholesterol and the transfer of cholesteryl ester from high-density lipoproteins (**HDL**s) toward very-low- and low-density lipoproteins (**VLDL**s+**LDL**s). Another transfer factor, phospholipid transfer protein (PLTP), recently has been shown to be involved in the interconversion of **HDL** particles in vitro, but its physiological function is not yet clear. We measured the activities of LCAT, CETP (as cholesteryl ester exchange activity), and PLTP using exogenous substrate assays as well as lipoprotein profiles in the plasma of 21 normolipidemic cigarette-**smoking** men (total plasma cholesterol below 6.5 mmol/L and triglyceride below 2.5 mmol/L) and 21 individually matched non**smoking** control subjects. **HDL** cholesterol, **HDL** cholesteryl ester, and plasma apolipoprotein A-I levels were lower in the smokers than in the control subjects (P < or = .05 for all parameters). Median plasma CETP activity was 18% higher (P < .02) and median plasma PLTP activity was 8% higher (P < .05) in the smokers compared with the nonsmokers. LCAT activity was not different between the groups. **HDL** cholesteryl ester concentration was positively related to LCAT activity in control subjects but not in smokers. By contrast, there was an inverse relation of CETP activity with **HDL** cholesteryl ester in smokers but not in nonsmokers. Multiple regression analysis demonstrated that the lowering effect of **smoking** on **HDL** cholesteryl ester could be explained by its influence on CETP activity.(ABSTRACT TRUNCATED AT 250 WORDS)

PM3000457397

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

113: Atherosclerosis 1994 Sep 30;110(1):13-23

Influence of lipoprotein lipids, dietary fat and smoking on macrophage degradation of native and oxidized low density lipoprotein.

Regnstrom J, Walldius G, Hadell K, Johansson J, Holme I, Olsson AG, Nilsson J

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Relatively little is known about the biological mechanisms by which lipoproteins promote atherogenesis. It has, however, been shown that structural modification of low density lipoprotein (**LDL**), such as by oxidation, results in their uptake and degradation by intimal macrophages and consequently leads to formation of lipid-rich atherosclerotic lesions. The aim of the present investigation was to study the influence of dietary intake of fat, lipoprotein lipid composition, **smoking** and gender on macrophage degradation of **LDL** before and after oxidation. The study group consisted of 48 males and 56 females with hyperlipidemia taking part in the open prerandomization phase of the Probucol Quantitative Regression Swedish Trial (PQRST). Analysis including lipoprotein determinations, dietary and **smoking** habit interviews, **LDL** degradation by macrophages, **LDL** receptor binding and **LDL** thiobarbituric acid reactive substance (**TBARS**) levels before and after copper ion-induced oxidation was done during the pre-andomization phase of the study. Increased plasma and very low density lipoprotein (V**LDL**) triglyceride levels were associated with an increased macrophage degradation of native **LDL**, whereas no such association was found after oxidation of **LDL**. The dietary intake of polyunsaturated fatty acids (PUFA) was also inversely related to the degradation of native **LDL** by macrophages, but increased the rate at which oxidized **LDL** was degraded. **Smoking** and gender did not influence the rate of macrophage degradation of native or oxidized **LDL**. It is concluded that hypertriglyceridemia is associated with an increased macrophage degradation of **LDL**. This may represent a mechanism by which hypertriglyceridemia promotes atherosclerosis.

Publication Types:
Clinical trial

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

114: Am J Clin Nutr 1994 Sep;60(3):383-7

Vitamin E supplementation suppresses indexes of lipid peroxidation and platelet counts in blood of smokers and nonsmokers but plasma lipoprotein concentrations remain unchanged.

Brown KM, Morrice PC, Duthie GG

Rowett Research Institute, Bucksburn, Aberdeen, Scotland, UK.

Smokers incur a sustained free radical load that may increase their vitamin E requirement. Erythrocytes of male smokers from a Scottish population with a habitually low vitamin E intake were more susceptible to hydrogen peroxide-stimulated peroxidation than were those from nonsmokers ($P < 0.001$). Plasma concentrations of lipid peroxides, thiobarbituric acid reactive substances, and conjugated dienes were also elevated in smokers compared with nonsmokers ($P < 0.05$). These indexes of oxidative stress were markedly decreased ($P < 0.001$) in the smokers and nonsmokers after consumption of 280 mg dl-alpha tocopherol acetate/d for 10 wk. Platelet numbers in serum of both smokers and nonsmokers were also decreased by vitamin E supplementation ($P < 0.02$). Although the clinical significance of the results is unclear, elevated indexes of lipid peroxidation are associated with the pathogenesis of atherosclerosis, and platelets are involved with fibrinolysis. Therefore, both smokers and non-smokers may benefit from increased vitamin E intakes.

115: Am J Physiol 1994 Apr;266(4 Pt 1):L382-8

Humic-like substances in cigarette smoke condensate and lung tissue of smokers.

Ghio AJ, Stonehuerner J, Quigley DR

Durham Veterans Affairs Medical Center, North Carolina.

Deposition of pigmented matter in the lower respiratory tract correlates with the extent of emphysema in smokers as well as with free radical generation and iron accumulation. Pulmonary emphysema is postulated to be mediated by free radical generation which is either directly or indirectly associated with cigarette smoke exposure. The hypothesis was tested that 1) incomplete combustion of tobacco yields humic-like substances (HLS) which 2) deposit in the lung as pigmented particulates, 3) complex iron cations in vitro and in vivo, and 4) have a capacity to catalyze oxidant formation. HLS, isolated by alkali extraction of cigarette smoke condensate (CSC) (Tobacco Health Research Institute, University of Kentucky), demonstrated a high carbon and low carboxylate content on elemental and functional group analyses, respectively, compared with values for HLS sequestered from soils. The HLS isolated from CSC had a capacity to complex iron in vitro and accumulated the metal in vivo after intratracheal instillation in an animal model. Both HLS and its iron complex generated free radicals, and some portion of this oxidant generation was metal dependent. Lung tissue collected at autopsy from smokers contained HLS with an infrared spectrum almost identical to that of the material isolated from CSC. Associations between particulate deposition, metal accumulation, and free radical generation suggest a possible role of HLS in the induction of lung disease following cigarette exposure.

PM3000457399

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

116: Prev Med 1994 Mar;23(2):190-6

Cholesterol changes in smoking cessation using the transdermal nicotine system.Transdermal Nicotine Study Group.

Allen SS, Hatsukami D, Gorsline J

Department of Family Practice and Community Health, Medical School, University of Minnesota, Minneapolis 55455.

BACKGROUND. Cigarette **smoking** is a well-known major risk factor in coronary heart disease. **Smoking** cessation results in a positive change in atherogenic factors. High-density lipoprotein cholesterol has been observed as increasing with **smoking** cessation. Since the use of nicotine transdermal replacement has become so widespread, this study examined the effect, if any, of the transdermal nicotine system on selected cardiovascular parameters in patients who were abstinent from cigarette **smoking**, and possible dose effect. METHODS. Eight cardiovascular outcome measures were evaluated at baseline and Week 6 in both abstinent and non-abstinent patients randomized to four treatment groups; transdermal nicotine system 7 mg, 14 mg, and 21 mg per day, and placebos. RESULTS. In abstinent patients, systolic blood pressure and heart rate decreased from baseline (while still **smoking**, before the start of the study) to the end of transdermal treatment, while weight increased. Similarly, **HDL** increased while **LDL** decreased and triglycerides increased. In nonabstinent patients, weight also increased from baseline to Week 6 while heart rate decreased. No other variables showed significant change. In abstinent patients, effect of nicotine dosage was observed with greater weight gain in placebo than 21 mg TTS patients and greater decrease in heart rate in placebo than 21 mg TTS patients. CONCLUSIONS. In summary, the abstinent patients showed a positive effect of **smoking** cessation on cardiovascular risk factors even while using the transdermal nicotine system. These findings are favorable since the transdermal nicotine system has become a useful method of nicotine replacement in **smoking** cessation programs.

Publication Types:
Clinical trial
Multicenter study
Randomized controlled trial

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

117: Arterioscler Thromb 1994 Mar;14(3):336-44

Regulation of plasma HDL cholesterol and subfraction distribution by genetic and environmental factors. Associations between the TaqI B RFLP in the CETP gene and smoking and obesity.

Freeman DJ, Griffin BA, Holmes AP, Lindsay GM, Gaffney D, Packard CJ, Shepherd J

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This study investigated in a healthy population (n = 220) the association of the TaqI B restriction fragment length polymorphism (RFLP) in the cholesteryl ester transfer protein (CETP) gene with plasma high-density lipoprotein (**HDL**) cholesterol concentration and subfraction distribution. A raised **HDL** cholesterol level was found in B2B2 homozygotes (B2 cutting site absent) and was associated specifically with a 45% increase in **HDL**2 compared with B1B1 homozygotes (B1B1, 77 +/- 39 mg/100 mL, mean +/- SD; B2B2, 112 +/- 59 mg/100 mL; P < 0.01). Total plasma, very-low-density lipoprotein, and **HDL** triglyceride levels did not differ among the genotype groups, nor did plasma apolipoprotein AI levels (B1B1, 1.45 +/- 0.35 mg/mL, mean +/- SD; B2B2, 1.56 +/- 0.33 mg/mL). Thus, the genetic variation appeared to be independent of metabolic factors that are known to regulate **HDL** levels. Plasma CETP exchange activity was unlikely to be the cause of the association, since it did not differ between genotype groups and was not correlated with **HDL**2 concentration. Multivariate analysis demonstrated that the TaqI B polymorphism had an effect on **HDL** cholesterol and **HDL**2 that was independent of age, sex, body mass index, oral contraceptive use, exercise, alcohol consumption, and plasma triglycerides. In smokers, the presence of the B2B2 genotype did not result in increased **HDL** cholesterol or **HDL**2, whereas in obese subjects, the difference between B1B1 and B2B2 individuals was diminished. We conclude that the TaqI B RFLP is associated with a antitatively significant effect on plasma **HDL**2 levels that is independent of plasma triglycerides and interacts with lifestyle factors.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

118: Genet Epidemiol 1994;11(3):255-64

Guanidine to adenine (G/A) substitution in the promoter region of the apolipoprotein AI gene is associated with elevated serum apolipoprotein AI levels in Chinese non-smokers.

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Department of Paediatrics, National University of Singapore.

The influence of the guanidine to adenine (G/A) substitution in the promoter region of the apolipoprotein (apo) AI gene (at -75 bp) on serum lipids and apolipoproteins was studied in 287 healthy Chinese of both sexes in Singapore. Women had significantly higher levels of high-density lipoprotein cholesterol (**HDL**C) and apo AI and lower low-density lipoprotein cholesterol (**LDL**C). The distribution of genotypes was at Hardy-Weinberg equilibrium. The frequency of the A allele in the Chinese was significantly higher [0.27; 95% confidence interval (CI) 0.24-0.31] than that reported in Caucasians (0.12; 95% CI 0.09-0.14). In men, the A allele was associated with 20% higher apo AI; this association was completely absent in women. Furthermore, in men this association was only observed in those who had never smoked, and was absent in smokers. The G/A substitution explained 9% ($P < 0.02$) of the sample variance of apo AI in non-**smoking** men. The modulating influence of **smoking** could not be examined in women because too few women smoke. Although the impact of this polymorphism is modulated by hormones and **smoking**, it is of importance in determining levels of apo AI in healthy Chinese individuals. No association of the G/A substitution of the apo AI gene was observed with any other lipid traits.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

119: Diabetologia 1993 Dec;36(12):1275-81

Hyperinsulinaemia, dyslipidaemia and exaggerated adrenal androgen response to adrenocorticotropin in male smokers.

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Insulin resistance and dyslipidaemia associated with **smoking** may result from increased secretion of anti-insulin hormones. We compared the pituitary-adrenocortical function using oral glucose tolerance, dexamethasone suppression and ACTH stimulation tests in **smoking** (n = 22) and non-**smoking** (n = 22) healthy males matched for age, body mass index, and waist-to-hip ratio. Smokers had lower **HDL**-cholesterol ($p < 0.02$), and higher triglyceride ($p < 0.001$), basal cortisol ($p < 0.05$), insulin ($p < 0.05$), and C-peptide ($p < 0.02$) levels, and a higher response of insulin and C-peptide to oral glucose ($p < 0.005$) than non-smokers, while the ACTH, cortisol, 17-hydroxyprogesterone, dehydroepiandrosterone, and androstenedione responses to oral glucose were similar in both groups. No differences were found in the response of cortisol, 17-hydroxyprogesterone, dehydroepiandrosterone, and androstenedione to dexamethasone. In contrast, the response of 17-hydroxyprogesterone ($p = 0.04$), dehydroepiandrosterone ($p = 0.007$), and androstenedione ($p = 0.001$) to ACTH was higher in smokers than non-smokers, while the increase in cortisol was of marginal significance ($p = 0.07$). In multiple regression analyses the dehydroepiandrosterone response to ACTH was a significant determinant of insulin, C-peptide, and triglyceride levels independent of physical activity, waist-to-hip ratio and **HDL**-cholesterol. Thus, **smoking** inhibits the adrenal 21-hydroxylase resulting in an increase in the production of adrenal androgens, which might contribute to the insulin resistance and dyslipidaemia in smokers.

PM3000457403

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

120: Int J Epidemiol 1993 Dec;22(6):1048-55

Cardiovascular risk factors in the Republic of Karelia, Russia, and in North Karelia, Finland.

Puska P, Matilainen T, Jousilahti P, Korhonen H, Vartiainen E, Pokusajeva S, Moisejeva N, Uhanov M, Kallio I, Artemjev A

National Public Health Institute, Department of Epidemiology and Health Promotion, Helsinki, Finland.

Cardiovascular disease risk factors were measured in a population survey in Pitkaranta District in the Republic of Karelia and in North Karelia in Finland in spring 1992. According to official statistics the cardiovascular mortality in the Republic of Karelia is somewhat higher, and total mortality and cancer mortality considerably higher than in North Karelia. A random sample of the population, aged 25-64 years, was taken in Pitkaranta (n = 1000) and in North Karelia (n = 2000). The participation rates were 84% and 74% respectively. The mean total serum cholesterol among men was 5.2 mmol/l in Pitkaranta and 5.8 mmol/l in North Karelia ($P < 0.001$) and among women 5.3 mmol/l and 5.6 mmol/l ($P < 0.001$), respectively. The mean **high density lipoprotein** (**HDL**) cholesterol levels among men were 1.4 mmol/l and 1.3 mmol/l ($P < 0.001$), and among women 1.4 mmol/l and 1.5 mmol/l ($P < 0.001$), respectively. There were no significant differences in blood pressure among men, but women in Pitkaranta had higher blood pressure than women in North Karelia. The mean body mass index in Pitkaranta was higher among women, 28.0 versus 26.5 ($P < 0.001$) and lower among men, 25.2 versus 27.0 ($P < 0.001$) than in North Karelia. **Smoking** was much more common among men (65% versus 31%) but less common among women (10% versus 16%) in Pitkaranta than in North Karelia. The general level of the risk factors, and especially the higher prevalence of **smoking** among men could explain the high mortality rates in Pitkaranta, and in particular the high cancer mortality.

121: Jpn Heart J 1993 Nov;34(6):759-62

Cigarette smoking and lipids and lipoproteins in cord plasma.

Adam B, Cetinkaya F, Malatyalioglu E, Gurses N

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The effects of **smoking** on maternal and cord plasma lipid and lipoprotein levels were measured in 40 smoker mothers and their newborns and compared to nonsmokers. Significantly higher levels of total cholesterol, low density lipoprotein cholesterol and very low density lipoprotein cholesterol and lower levels of high density lipoprotein cholesterol were found in smoker mothers and their newborns in comparison to nonsmokers. These results suggest that **smoking** does not affect only the lipids and lipoproteins of pregnant women but also those of their fetuses.

PM3000457404

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

122: Eur J Clin Invest 1993 Oct;23(10):630-40

Smoking and plasma lipoproteins in man: effects on low density lipoprotein cholesterol levels and high density lipoprotein subfraction distribution.

Freeman DJ, Griffin BA, Murray E, Lindsay GM, Gaffney D, Packard CJ, Shepherd J

Institute of Biochemistry, Royal Infirmary, Glasgow, UK.

In a survey of a healthy population (n = 197), **LDL** cholesterol, plasma triglycerides and V**LDL** triglycerides were found to be substantially increased and plasma **HDL** cholesterol decreased in smokers. The lipid-associated atherogenic risk in smokers as assessed by the **LDL/HDL** ratio was significantly higher [2.89 (SD 1.18, n = 63)] than in non-smokers [2.38 (SD 0.98, n = 86) P < 0.01]. The lower **HDL** level found in smokers was explained by a lower **HDL**-2 subfraction as determined by analytical ultracentrifugation. **HDL** 2b, 2a and 3a, measured by gradient gel electrophoresis, were all lower in the smokers but this was only significant for **HDL** 2a. **Smoking** had no effect on Lp(a) levels. **HDL** cholesterol and **HDL**-2 were strongly negatively correlated whereas **LDL** cholesterol and **LDL/HDL** ratio were strongly positively correlated with the plasma triglyceride concentration. There was a small but significant reduction in plasma CETP activity [non-smokers 49% t/microliter (SD 17, n = 90), smokers 43% t/microliter (SD 17, n = 66) P < 0.05] but CETP activity was not correlated with any measure of **HDL** in this population. **Smoking** was found to be an important independent contributor to the variation in plasma triglyceride, **HDL**, **HDL**-2 and **LDL/HDL** ratio. After correcting for sex, age, BMI, alcohol consumption, oral contraceptive use and plasma triglycerides **smoking** was still found to be significantly associated with **HDL** and the **LDL/HDL** ratio. Upon adjustment for covariant factors the mean differences between smokers and non-smokers for **HDL** cholesterol, **HDL**-2 and **LDL/HDL** were 0.15 mM, 16 mg dl-1 and 0.39 respectively. There appeared to be important sex differences in the influence of **smoking** on plasma lipoproteins. In women the main impact of **smoking** was on triglyceride levels and they in turn affected **LDL** and **HDL**. In contrast, in men, **smoking** had little impact on triglycerides and affected **HDL** more directly. We conclude that **smoking** cigarettes has an important effect on plasma lipoprotein metabolism through multiple mechanisms.

PM3000457405

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

123: J Am Coll Cardiol 1993 Oct;22(4):1159-67

Nicotine effects on eicosanoid formation and hemostatic function: comparison of transdermal nicotine and cigarette smoking.

Benowitz NL, Fitzgerald GA, Wilson M, Zhang Q

Division of Clinical Pharmacology and Experimental Therapeutics, San Francisco General Hospital Medical Center, California 94110.

OBJECTIVES. The purpose of this study was to examine the possible role of nicotine in enhancing coagulation and to assess the potential cardiovascular toxicity of transdermal nicotine therapy for **smoking** cessation. BACKGROUND. Cigarette **smoking** increases the risks of acute coronary events. A likely contributing mechanism is activation of coagulation. The role of nicotine in enhancing coagulability has not been resolved. METHODS. We compared in a crossover study the effects of cigarette **smoking**, transdermal nicotine and placebo transdermal nicotine, each for 5 days, in 12 healthy smokers. RESULTS. Cigarette **smoking** increased the urinary excretion of 11-dehydro-**thromboxane B2** (reflecting thromboxane A2 generation) and increased plasma concentration of the platelet alpha-granule constituents, platelet factor 4 and beta-thromboglobulin, compared with placebo treatment, indicating in vivo platelet activation. Cigarette **smoking** was also associated with higher levels of **fibrinogen** in plasma. Transdermal nicotine produced plasma levels of nicotine in the same range as those during **smoking** but had no effect on thromboxane A2 metabolite excretion, platelet alpha-granule release or plasma **fibrinogen**, compared with placebo. Excretion of 2,3-dinor-6-keto-PGF1 alpha (reflecting prostacyclin generation) was not significantly influenced by any treatment. These results suggest that nicotine as such is not responsible for the platelet activation or elevation of plasma **fibrinogen** seen in smokers. However, we cannot exclude the possibility that intermittent bolus-like dosing of nicotine from cigarettes could have different effects from those produced by continually released transdermal nicotine. Other findings were that cigarette **smoking** and transdermal nicotine treatment were both associated with a higher white blood cell count compared with the placebo patch condition, suggesting a direct effect of nicotine to increase circulating white cells. Factor VII coagulant activity (VIIc) was significantly lower during cigarette **smoking**, than during either nicotine or placebo patch conditions. CONCLUSIONS. Transdermal nicotine has less effect on platelet activation and catecholamine release than does cigarette **smoking**, and its use in **smoking** cessation treatment of patients with coronary heart disease is likely to be safer than cigarette **smoking**.

Publication Types:
Clinical trial
Controlled clinical trial

Comments:
Comment in: J Am Coll Cardiol 1993 Oct;22(4):1168-9

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

124: Int J Epidemiol 1993 Aug;22(4):637-43
Relationships between cigarette smoking, blood pressure and serum lipids in the Singapore general population.

Hughes K, Leong WP, Sothy SP, Lun KC, Yeo PP

Department of Community, Occupational and Family Medicine, National University of Singapore.

In a cross-sectional random survey of the whole of Singapore (2143 subjects aged 18-69 years), cardiovascular risk factors were measured by standardized techniques. For the analysis in the 18-69 year age group there was adjustment for ethnic group, age, body mass index, alcohol consumption and physical activity. Among serum lipids, **high density lipoprotein** (**HDL**-) cholesterol and fasting triglyceride were inversely related with partial correlation coefficients (r) of males -0.34 ($P < 0.001$) and females -0.26 ($P < 0.001$). There were no relationships between blood pressure and serum lipids except for direct ones with fasting triglyceride, being males (systolic $r = 0.06$, $P = 0.066$ and diastolic $r = 0.12$, $P < 0.001$) and females (systolic $r = 0.11$, $P < 0.001$ and diastolic $r = 0.13$, $P < 0.001$). Cigarette **smoking**, in males, was related to systolic blood pressure (inversely), with, compared to non-smokers, a reduction of 1.3 mm Hg (1.1%) in light smokers, 3.8 mm Hg (3.1%) in moderate smokers and 4.6 mm Hg (3.7%) in heavy smokers; there was no clear relation with diastolic blood pressure. Cigarette **smoking**, in males, was related to **HDL**-cholesterol (inversely), even after further adjustment for fasting triglyceride, with compared to non-smokers reductions of 0.03 mmol/l (3.4%) in light smokers, 0.09 mmol/l (10.3%) in moderate smokers and 0.12 mmol/l (13.8%) in heavy smokers. Cigarette **smoking** was related to fasting triglyceride (directly) but this was removed by further adjustment for **HDL**-cholesterol. Cigarette **smoking** was not related to low density lipoprotein cholesterol. These results are compared to those of other surveys.

125: Ann N Y Acad Sci 1993 May 28;686:120-9
Cigarette smoking, antioxidants, lipid peroxidation, and coronary heart disease.

Duthie GG, Arthur JR, Beattie JA, Brown KM, Morrice PC, Robertson JD, Shortt CT, Walker KA, James WP

Rowett Research Institute, Aberdeen, Scotland.

PM3000457407

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

126: Prostaglandins 1993 May;45(5):401-11
Urinary excretion and origin of 11-dehydro-2,3-dinor-thromboxane B2 in man.

Chiabrando C, Rivoltella L, Alberti E, Bonollo M, Djurup R, Fanelli R
Istituto di Ricerche Farmacologiche Mario Negri, Milano, Italy.

The in vivo biosynthesis of **thromboxane B2** (**TXB2**) in man is currently evaluated by measuring urinary excretion of its major urinary metabolites, 11-dehydro-**TXB2** and 2,3-dinor-**TXB2**. 11-Dehydro-2,3-dinor-**TXB2**, another prominent metabolite of exogenous **TXB2** in man, has never been measured in human urine. We measured urinary 11-dehydro-2,3-dinor-**TXB2** in parallel with 11-dehydro-**TXB2** and 2,3-dinor-**TXB2** by immunoaffinity extraction/gas chromatography-mass spectrometry in healthy non-smokers (n = 12) and age-matched smokers (n = 11). In non-smokers, urinary excretion of 11-dehydro-2,3-dinor-**TXB2**, 11-dehydro-**TXB2** and 2,3-dinor-**TXB2** was 29.7 +/- 11.1, 53.6 +/- 15.0 and 13.5 +/- 2.8 ng/h (mean +/- SD), respectively. In smokers, only urinary excretion of 2,3-dinor-**TXB2** was significantly different (19.7 +/- 6.7 ng/h, $p < 0.01$). Selective inhibition of platelet thromboxane biosynthesis by chronic low-dose aspirin (30 mg/day for 8 days, 4 subjects) comparably reduced platelet-derived metabolites and 11-dehydro-2,3-dinor-**TXB2**, suggesting that the latter also derives from platelets in healthy subjects.

127: Eur J Med 1993 Apr;2(4):205-8
Age, sex, cigarette smoking and indices of free radical activity in healthy humans.

Bridges AB, Scott NA, Parry GJ, Belch JJ
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OBJECTIVES: To determine the effect of age, sex and **smoking** on free radical (FR)indices. There is currently considerable research interest into the role of FRsin the pathogenesis of many diseases and it is therefore important to identify factors in healthy subjects which influence the markers used to assess FR activity. METHODS: Blood samples were obtained from 123 healthy subjects whose age, sex and **smoking** habits were recorded. The following were measured on each sample: **malondialdehyde** (MDA) which is a product of FR mediated lipid peroxidation and the FR scavengers plasma thiols (PSH), red cell glutathione (GSH) and superoxide dismutase (SOD). RESULTS: **Malondialdehyde** levels were significantly increased in cigarette smokers ($p < 0.02$) but no significant age related increase in MDA was detected for the group as a whole. However, female smokers had the highest rate of MDA increase with age followed by male smokers and female non-smokers. MDA levels of male non-smokers were unaffected by age. A significant negative correlation was detected between PSH and age ($p < 0.001$). GSH was significantly higher in females ($p < 0.05$) and the red cell content of GSH and SOD were significantly inversely related ($p < 0.01$). CONCLUSION: This study of normal subjects describes an age related increase in **malondialdehyde** levels, the rate of which is influenced by sex and **smoking** status. In humans, plasma thiol levels decrease with increasing age, females have higher red cell glutathione and there is a significant inverse relationship between red blood cell superoxide dismutase and glutathione levels. Furthermore, cigarette **smoking** increases plasma **malondialdehyde** levels. With the considerable current interest in free radicals, it is important to identify factors which influence the indices used to assess free radical activity in disease states.

PM3000457408

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

128: Eur J Epidemiol 1993 Mar;9(2):140-50
The relationship between coffee consumption and serum cholesterol under consideration of smoking history.

Mensink GB, Kohlmeier L, Rehm J, Hoffmeister H
Institute for Social Medicine and Epidemiology, Federal Health Office, Berlin, Federal Republic of Germany.

A large German population sample of 6820 men and 7258 women was used to investigate the relationship between coffee consumption, total serum cholesterol and **HDL** cholesterol. Analyses were conducted on men and women separately. Differences in age, body mass index, diastolic blood pressure, **smoking** habits, alcohol, fish, milk and tea consumption, physical activity and medication use were controlled for in the analyses. Interactions between coffee consumption and **smoking** habits in their relationship with serum cholesterol were part of the analyses. For men, a positive relationship between coffee consumption and total serum cholesterol was found among smokers and life-long abstainers but not in the group of ex-smokers. In women a relationship between coffee consumption and total serum cholesterol was also present, but very weak (only statistical significant in covariance analyses). Levels of **HDL** cholesterol did not correlate with coffee consumption in either men and women. Hypotheses concerning the peculiarities of the group of ex-smokers are developed, and supporting empirical evidence is given. It is suggested that the group of ex-smokers should always be analysed separately.

129: Nagoya J Med Sci 1993 Mar;55(1-4):65-70
The relationship of high-density lipoprotein cholesterol to obesity, drinking and smoking habits.

Miyao M, Furuta M, Kondo T, Sakakibara H, Ishihara S, Yamanaka K, Yamada S

Department of Public Health, Nagoya University School of Medicine, Japan.

Subjects were a total of 726 Japanese male transport service workers between the ages of 35 and 50. They were analyzed for obesity and drinking or **smoking** habits in relation to their **HDL**-cholesterol level and total cholesterol concentration. The cases were 100 low **HDL**-cholesterol (less than 40 mg/dl) and 121 high total cholesterol (greater than 230 mg/dl) subjects. We used a multiple logistic regression analysis. As for abnormally high total cholesterol, it was determined that the odds ratios at 40, 45, and 50 years of age were 1.95, 2.23, and 2.65, respectively, when 35-year-olds were considered the baseline. Abnormally high total cholesterol showed an odds ratio of 0.27 among thin subjects with a Body Mass Index (BMI) less than 21.0, when subjects with a standard BMI were calculated as the baseline. With reference to low **HDL**-cholesterol, the odds ratio for lean subjects was 0.30 against those who had standard habitus, while subjects with a BMI of more than 25.1 had an odds ratio of more than double. Compared with nondrinkers, low **HDL**-cholesterol exhibited odds ratios of 0.16 and 0.23, respectively, for moderate and heavy drinkers. In cases of low **HDL**-cholesterol, the odds ratios for mild and heavy smokers were 1.91 and 2.27, respectively, versus nonsmokers.

PM3000457409

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

130: Scand J Soc Med 1992 Dec;20(4):196-203

Coronary risk factors in middle-aged men as related to smoking, coffee intake and physical activity.

Hostmark AT, Berg J, Brudal S, Berge SR, Kierulf P, Bjerkedal T

Department of Preventive Medicine, University of Oslo.

The relationship between lifestyle and coronary risk factors in blood was investigated in 165 middle-aged men. Plasma **fibrinogen**, serum triacylglycerols (TG), and apolipoprotein B (apo B) were higher, and high density lipoprotein cholesterol (**HDL**c) lower in smokers (n = 69) than in non-smokers (n = 96). By linear regression analysis there was a significant positive association between degree of **smoking** and either total cholesterol (TC), apo B, or plasma **fibrinogen**, whereas **smoking** was inversely related to **HDL**c. **Smoking** and coffee intake were positively correlated with an atherogenic index, reflecting the balance between low and high density lipoproteins. Sedentary men (n = 59) had higher mean TC, apo B, and atherogenic index than physically active men (n = 104). Smokers used salt more often than non-smokers. Physically active men used vegetables more often than sedentary men. Combining several habits into a "bad habit" score gave a high level of significance for its association with TC, apo B, and the atherogenic index. The results indicate that lifestyle may influence several blood factors involved in atherosclerosis development.

131: J Med Assoc Thai 1992 Dec;75(12):709-13

Serum lipid, lipoprotein-cholesterol and apolipoproteins A-I and B of smoking and non-smoking males.

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Department of Clinical Chemistry, Faculty of Medical Technology, Mahidol University, Bangkok, Thailand.

Cigarette **smoking** is an important risk factor for coronary heart disease, stroke and peripheral vascular disease. Accordingly, we measured the serum lipid, lipoprotein-cholesterol and apolipoprotein A-I, B in 128 cigarette **smoking** males and 67 non-**smoking** males. The total cholesterol and **LDL**-cholesterol in smokers and non-smokers showed no statistical significance. The smokers had significantly higher serum triglyceride and **VLDL**-cholesterol levels ($P < 0.001$), but significantly lower **HDL**-cholesterol levels ($P < 0.05$) than non-smokers. The apolipoprotein A-I was significantly lower and apolipoprotein B was significantly higher in smokers than non-smokers ($P < 0.001$). Levels of lipid, lipoprotein-cholesterol were related to the number of cigarettes smoked per day. Triglyceride and **VLDL**-cholesterol levels were significantly higher in those who smoked > 20 cigarettes/day compared with those who smoked 10-20, < 10 cigarettes/day and non-smokers ($P < 0.05$). Those who smoked > 20 cigarettes/day had significantly lower **HDL**-cholesterol than those of non-smokers ($P < 0.05$). All three groups of smokers had significantly lower apolipoprotein A-I than non-smokers ($P < 0.05$), whereas, those who smoked > 20 cigarettes/day had significantly higher apolipoprotein B levels than those who smoked 10-20, < 10 cigarettes/day and non-smokers ($P < 0.05$).

PM3000457410

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

132: Thromb Haemost 1992 Nov 10;68(5):583-8

Cigarette smoking increases thromboxane A2 formation without affecting platelet survival in young healthy females.

Dotevall A, Rangemark C, Eriksson E, Kutti J, Wadenvik H, Wennmalm A

Department of Medicine, Ostra Hospital, Goteborg, Sweden.

Smoking is a risk factor for the development of atherosclerotic cardiovascular disease, in men as well as in women. An increased urinary excretion of the thromboxane metabolite 2,3-dinorthromboxane B2 (Tx-M) has been observed in smokers of both genders, suggesting that cigarette **smoking** may facilitate cardiovascular disease via an action on the platelets. The present study addressed the hypothesis that the increased Tx-M excretion in female smokers reflects a true facilitation of platelet reactivity in vivo, rather than an increased destruction of the platelets. In healthy female volunteers (aged 20-46 years, 18 smokers and 17 non-smokers) platelet life-span and indices of platelet activity were determined, together with plasma levels of plasminogen activator inhibitor-1 (PAI-1), **fibrinogen**, peripheral blood cell counts and hematocrit. The urinary excretion of Tx-M was higher in smokers than in non-smokers (361 vs. 204 pg/mg creatinine, respectively, $p < 0.05$), while plasma and urinary beta-thromboglobulin, plasma platelet factor 4, platelet mean life-span and platelet production rate did not differ between the groups. PAI-1 activity, white blood cell count and hematocrit were higher in smokers than in non-smokers ($p < 0.05$). These data indicate that **smoking** facilitates platelet formation of thromboxane A2 without affecting platelet survival; i.e. it increases the activity of platelets without affecting their viability to a measurable extent. Such an increase in platelet activity, operating in parallel to a reduced fibrinolytic activity and a higher hematocrit and white blood cell count, may play an etiological role in **smoking**-induced cardiovascular disease in women.

PM3000457411

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

133: Circulation 1992 Nov;86(5):1495-500
Tobacco use and urinary excretion of thromboxane A2 and prostacyclin metabolites in women stratified by age.

Rangemark C, Benthin G, Granstrom EF, Persson L, Winell S, Wennmalm A

Department of Clinical Physiology, Gothenburg University, Sweden.

BACKGROUND. Activated platelets have been implicated in both acute thrombus formation and atherogenesis. Because **smoking** is a risk factor for cardiovascular disease in men and women and male smokers have biochemical evidence of increased platelet activation, we found it of interest to study whether **smoking** augments platelet activity in women as well. METHODS AND RESULTS. Data on **smoking** habits and a urinary sample were obtained from 125 healthy female nonsmokers and an equal number of smokers, stratified by age in five groups from 18 to 59 years old. Urinary samples were analyzed with gas chromatography/mass spectrometry for the 2,3-dinormetabolites of thromboxane A2 (Tx-M), reflecting platelet activity, and prostacyclin (PGI-M), representing platelet/vessel wall interaction. Urinary Tx-M in smokers was higher than in nonsmokers ($p < 0.001$), increasing with the number of cigarettes smoked per day and with age. In nonsmokers, there was no difference in Tx-M between the age groups. Urinary PGI-M in smokers was higher than that in nonsmokers ($p < 0.001$) and decreased with age in nonsmokers but not in smokers. There was no difference in Tx-M between previous smokers and lifelong nonsmokers. CONCLUSIONS. The elevated Tx-M in women who smoke cigarettes indicates an increased platelet activity that is dependent on **smoking** intensity. In parallel, PGI-M is augmented, suggesting that platelet/vessel wall interaction is stimulated. Quitting **smoking** is an effective means to restore platelet function. We propose that the observed increase in platelet activity in women who smoke cigarettes may be related to subsequent development of cardiovascular disease and that quitting **smoking** should be considered a high-priority medical target also in this sex.

134: Indian J Med Res 1992 Oct;96:282-7
Serum lipids & lipoprotein profiles of cigarette smokers & passive smokers.

Whig J, Singh CB, Soni GL, Bansal AK

Department of Medicine, Dayanand Medical College & Hospital, Ludhiana.

Serum lipids and lipoproteins of 50 active and passive smokers were compared with levels in 25 control subjects. Active **smoking** resulted in an increase in total cholesterol (Tc) and triglycerides (Tg) as compared to control group. The passive smokers also showed relatively higher levels but the effect was not significant. Active **smoking** raised the low density lipoprotein cholesterol (**LDL**c) and very low density lipoprotein cholesterol (V**LDL**c) levels whereas high density lipoprotein cholesterol (**HDL**c) content was lowered, thus resulting in decreased ratios of **HDL**c/Tc and **HDL**c/**LDL**c. The passive smokers also showed slightly higher levels of **LDL**c and V**LDL**c but lower levels of **HDL**c, and a lower **HDL**c/**LDL**c ratio. Our findings suggest that **smoking** alters the serum lipids and lipoproteins and these changes are related to the duration and amount of **smoking**.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

135: Sci Total Environ 1992 Sep 25;126(3):209-29

Association of selected social, environmental and constitutional factors to blood lead levels in men aged 55-75 years.

Morisi G, Menditto A, Spagnolo A, Patriarca M, Menotti A

Laboratorio di Biochimica Clinica, Istituto Superiore di Sanita, Roma, Italy.

Blood lead (B-Pb) levels were determined in 1802 out of 1856 non-occupationally exposed men aged 55-75 years living in the Rome area who participated, between 1989 and 1990, in an epidemiological survey for coronary heart disease (New Risk Factors Project). The median B-Pb level was 113 micrograms/l (10th-90th centiles: 74-180 micrograms/l) and only 0.7 per cent (n = 14) of the subjects had B-Pb values higher than 300 micrograms/l. B-Pb levels were significantly and positively associated to alcohol consumption. Moderate and heavy drinkers had median B-Pb level of 143 micrograms/l (10th-90th centiles: 92-233) and 165 micrograms/l (10th-90th centiles: 102-285) respectively, whereas non-drinkers had a median B-Pb level of 96 micrograms/l (10th-90th centiles: 66-143). The influence of **smoking** habits was less relevant. Subjects who never smoked and subjects **smoking** more than 20 cigarettes daily had median B-Pb levels of 103 and 133 micrograms/l, respectively. Individuals classified as habitual car-drivers had slightly higher Pb levels than non-drivers. Subjects classified as manual workers had higher B-Pb levels in comparison with non-manual workers and retired subjects. B-Pb levels were directly related to **HDL**-cholesterol (**HDL**-C, r = 0.2252) and gamma-glutamyltransferase (gamma-GT, r = 0.2207) serum levels. The alleged alcohol consumption was more related to B-Pb level (r = 0.3848) than to serum level of **HDL**-C (r = 0.2474) or gamma-GT (r = 0.2469). A significant correlation (r = 0.2409) also existed between B-Pb and blood cadmium levels (B-Cd). Subjects with a low Gaensler ratio, an index of respiratory function, had higher B-Pb levels. In multiple regression analyses alcohol intake was the most important predictor of B-Pb level, explaining more (14.27%) of the total variance than did B-Cd (4.98%), **HDL**-C (1.89%), driving habits (1.46%), gamma-GT (1.09%), skinfold thickness (0.96%), and Gaensler index (0.38%). The risk ratio of having B-Pb level higher than 180 micrograms/l (90th centile of B-Pb distribution in our subjects) was 5.3 (95% CI: 2.7-10.4) for drinkers versus non-drinkers and 1.9 (95% CI: 1.2-3.1) for current smokers versus subjects who had never smoked. B-Pb was, at least in our subjects, a more specific and sensitive objective index of alcohol consumption than gamma-GT and **HDL**-C.(ABSTRACT TRUNCATED AT 400 WORDS)

PM3000457413

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

136: Jpn J Cancer Res 1992 Aug;83(8):806-11
Cigarette **smoking**, alcohol use and adenomatous polyps of the sigmoid colon.

Honjo S, Kono S, Shinchi K, Imanishi K, Hirohata T

Department of Public Health, School of Medicine, Kyushu University, Fukuoka.

The relationship of adenomatous polyps of the sigmoid colon with cigarette **smoking** and alcohol use was investigated in male self-defense officials in Japan. In the comparison between 116 cases and 930 controls, total ethanol intake was not at all associated with the risk of adenomatous polyps, but cigarette **smoking** was strongly related to adenomatous polyps. After adjustment for total ethanol intake, body mass index and rank, odds ratios (and 95% confidence interval) for the categories of 0, 1-399, 400-799, and 800 or more cigarette-years were 1.0 (referent), 2.3 (1.1-4.6), 2.9 (1.5-5.4) and 3.2 (1.6-6.5), respectively. Among five alcoholic beverages (sake, shochu, beer, whiskey including brandy, and wine), only whiskey consumption was weakly related to the risk of adenomatous polyps. Because the present findings disagree with an earlier observation on self-defense officials, we examined the association with **smoking** and alcohol use separately for small (less than 5 mm) and large (greater than or equal to 5 mm) adenomas, combining data from these two studies. Cigarette **smoking** was more strongly associated with small adenomas while the positive association with certain alcoholic beverages were largely confined to large adenomas. These findings suggest that cigarette **smoking** and alcohol use may be linked with the development of adenoma at different stages of colon tumorigenesis.

137: Am Heart J 1992 Jul;124(1):32-8

Statistical analysis of clinical risk factors for coronary artery spasm: identification of the most important determinant.

Nobuyoshi M, Abe M, Nosaka H, Kimura T, Yokoi H, Hamasaki N, Shindo T, Kimura K, Nakamura T, Nakagawa Y, et al
Department of Cardiology, Kokura Memorial Hospital, Kitakyushu, Japan.

Coronary artery spasm plays an important role in acute ischemic events, and it has a close relationship with coronary atherosclerosis. Thus we attempted to determine the most significant risk factor for coronary artery spasm. Among 3000 consecutive patients who underwent coronary cineangiography with ergonovine maleate testing, 330 with typical angina pectoris (group 1) and 294 with old myocardial infarction (group 2) were studied. We divided each group into three or four subgroups according to the presence of fixed organic stenosis (FOS+) or a positive reaction to ergonovine maleate (coronary artery spasm [CAS]+). We examined the relationship between coronary artery spasm and eight coronary risk factors: age, sex, hypertension, diabetes mellitus, **smoking**, and serum cholesterol, uric acid, and high-density lipoprotein cholesterol levels. The proportion of smokers in the subgroups with CAS(+) was significantly higher than in the subgroups with CAS(-)(p less than 0.01). There was no correlation between **smoking** and fixed organic stenosis. According to the results of multiple regression analysis, there was a positive correlation between **smoking** and CAS(+) and between serum high-density lipoprotein cholesterol levels and CAS(+)(p less than 0.01). Thus we concluded that **smoking** is the most significant risk factor in discriminating between patients with and without coronary artery spasm.

PM3000457414

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

138: J Epidemiol Community Health 1992 Jun;46(3):197-202

Blood lipids: the relationship with alcohol intake, smoking, and body weight.

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STUDY OBJECTIVE--The aim was to assess the interrelationship between alcohol intake, cigarette **smoking**, body weight, and blood lipid concentrations. DESIGN--This was the cross sectional (screening) phase of a prospective study. The main outcome measure was the blood lipids (serum total cholesterol, **HDL** cholesterol, and triglycerides). SETTING--General practices in 24 towns (The British Regional Heart Study). SUBJECTS--Subjects were 7735 men aged 40-59 years, selected at random from the age-sex registers of one group practice in each of the 24 towns. RESULTS--Univariate analysis showed little association between alcohol intake and total cholesterol, a strong positive relation with **HDL** cholesterol, and a significant increase in triglycerides in heavy drinkers. A strong positive association between alcohol intake and body weight was present in non-smokers but not in moderate/heavy smokers. With the exception of **HDL** cholesterol, the relationships between alcohol intake and serum lipids were significantly different in smokers and non-smokers, apparently due to the opposing effect of **smoking** on blood lipids and body weight. Total cholesterol and triglycerides were significantly and positively associated with alcohol intake in non-smokers, the cholesterol association being largely mediated by the influence of alcohol on body weight. In smokers, no such association was seen: current smokers who were heavy drinkers or non-drinkers had the lowest mean cholesterol levels. CONCLUSIONS--The association between alcohol intake and body weight and alcohol intake and blood lipids are strongly conditioned by cigarette **smoking**. Simple standardisation for **smoking** in multivariate analyses may obscure the independent relationship with alcohol. These findings are of importance in studies seeking to relate alcohol intake, body weight, or cigarette **smoking** to blood lipid concentrations, or blood lipid concentration to morbidity or mortality.

139: Prostaglandins Leukot Essent Fatty Acids 1992 Jun;46(2):81-6

Cigarette smoking and platelet-vessel wall interactions.

Lassila R, Laustiola KE

Wihuri Research Institute, Helsinki, Finland.

Publication Types:
Review
Review, tutorial

PM3000457415

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

140: Lancet 1992 May 9;339(8802):1128-30
Published erratum appears in Lancet 1992 Jun 13;339(8807):1492
Insulin resistance and cigarette smoking.

Facchini FS, Hollenbeck CB, Jeppesen J, Chen YD, Reaven GM

Department of Medicine, Stanford University School of Medicine, California.

Cigarette **smoking** is associated with increases in plasma triglycerides and decreases in plasma high density-lipoprotein-cholesterol concentration. These changes not only increase risk of coronary heart disease but also are secondary to resistance to insulin-stimulated glucose uptake or hyperinsulinaemia. To see whether there is a relation between cigarette **smoking** and insulin-mediated glucose uptake we measured plasma lipid and lipoprotein concentrations, plasma glucose and insulin response to an oral glucose challenge, and insulin-mediated glucose uptake in 40 matched healthy volunteers (20 non-smokers, 20 smokers). Smokers had significantly higher mean (SEM) very-low-density-lipoprotein triglycerides (0.66 [0.10] vs 0.39 [0.03] mmol/l, p less than 0.02) and cholesterol (0.45 [0.06] vs 0.23 [0.04] mmol/l, p less than 0.005) concentrations and lower high-density-lipoprotein cholesterol concentrations (1.16 [0.05] vs 1.51 [0.08] mmol/l, p less than 0.001). Although plasma glucose concentrations in response to the oral glucose load were similar in the two groups, plasma insulin response of the smokers was significantly higher (p less than 0.001). Finally, smokers had higher steady-state plasma glucose concentrations in response to a continuous infusion of glucose, insulin, and somatostatin (8.4 [0.2] vs 5.0 [0.3] mmol/l, p less than 0.001), despite similar steady-state plasma insulin concentrations. The findings show that chronic cigarette smokers are insulin resistant, hyperinsulinaemic, and dyslipidaemic compared with a matched group of non-smokers, and may help to explain why **smoking** increases risk of coronary heart disease.

Comments:
Comment in: Lancet 1992 Jun 27;339(8809):1619-20

PM3000457416

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

141: Arterioscler Thromb 1992 May;12(5):554-62

Supplementation with vitamin E but not beta-carotene in vivo protects low density lipoprotein from lipid peroxidation in vitro. Effect of cigarette smoking.

Princen HM, van Poppel G, Vogelezang C, Buytenhek R, Kok FJ

Gaubius Laboratory IVVO-TNO, Zeist, The Netherlands.

Several lines of evidence suggest that oxidatively modified low density lipoprotein (**LDL**) is atherogenic and that antioxidants may protect **LDL** against oxidation. In addition, cigarette **smoking** is known to induce oxidant stress. We have examined the effect of ingestion of the antioxidants D,L-alpha-tocopherol (vitamin E) and beta-carotene and of **smoking** on the resistance of **LDL** against copper-mediated oxidation. Six healthy non**smoking** volunteers ingested 1,000 IU/day D,L-alpha-tocopherol acetate for 7 days. After vitamin E ingestion concentrations of alpha-tocopherol in plasma and **LDL** increased 3.0- and 2.4-fold, respectively. Simultaneously, the oxidation resistance of **LDL** was elevated significantly (+41%), and the rate of oxidation was decreased significantly (-19%). The increase in alpha-tocopherol content of **LDL** and the increase in resistance time were highly correlated (rs = 0.89, p = 0.014). Eight weeks after termination of the vitamin E intake, alpha-tocopherol concentrations in plasma and **LDL** and oxidation resistance of **LDL** had returned to baseline values. In smokers (n = 46), plasma levels of vitamin C (-26%) and concentrations of beta-carotene (-44%, -43%) and total carotenoids (-23%, -29%) in plasma and **LDL**, respectively, were significantly lower compared with nonsmokers (n = 23). No differences were found in alpha-tocopherol content of **LDL** and the susceptibility of **LDL** to lipid peroxidation in both groups. Supplementation of a group of smokers in a 14-week randomized, double-blind, placebo-controlled intervention trial with beta-carotene resulted in a 16.6- and 5.0-fold increase of **LDL** beta-carotene and total carotenoid content, respectively.(ABSTRACT TRUNCATED AT 250 WORDS)

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

142: Ann Intern Med 1992 Apr 15;116(8):636-40

Factors influencing gastroduodenal mucosal prostaglandin concentrations: roles of smoking and aging.

Cryer B, Lee E, Feldman M

Department of Veterans Affairs Medical Center, Dallas, Texas.

OBJECTIVE: To evaluate behavioral, demographic, clinical, and histologic variables that independently influence gastroduodenal mucosal prostaglandin concentrations. DESIGN: Prospective study. SETTING: A clinical research laboratory located in a Department of Veterans Affairs hospital. PATIENTS: Fifty-two healthy adults who had no history of peptic ulcer disease and who were not receiving nonsteroidal anti-inflammatory drugs. MEASUREMENTS: Mucosal biopsy specimens were obtained endoscopically from the stomach (body and antrum) and the duodenum (bulb and postbulbar area). Mucosal extracts from each of these four regions were assessed by radioimmunoassay to determine prostaglandin E2 and prostaglandin F2 alpha concentrations. Specimens were also examined histologically for inflammation and the presence of Helicobacter pylori. A multivariate linear regression model was used to determine which behavioral, demographic, and histologic variables significantly and independently influenced gastroduodenal mucosal prostaglandin concentrations. RESULTS: **Smoking** and older age were independently associated with lower prostaglandin concentrations in all four mucosal regions (P = 0.0001 to P = 0.05). Compared with results in young nonsmokers, mucosal prostaglandin concentrations were reduced by 70% to 80% in older smokers. Gender, alcohol use, endoscopic appearance, dyspeptic symptoms, mucosal inflammation, and the presence of H. pylori had no consistent effect on prostaglandin content. CONCLUSION: **Smoking** and older age are associated with significantly reduced gastric and duodenal prostaglandin concentrations. These observations may help explain the predisposition to ulcer disease in smokers and older persons.

PM3000457418

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

143: Chung Hua Liu Hsing Ping Hsueh Tsa Chih 1992 Apr;13(2):97-100
[Influence of smoking on cholesterol concentrations in serum lipo-protein of healthy subjects].
[Article in Chinese]

Zhang Y

Department of Epidemiology, Linyi Medical School, Shandong.

Sixty hundred and nineteen-seven smokers and 841 non-smokers among healthy male workers of 40-60 years of age were comparatively observed. Their housing environment and working conditions were similar. The results showed that **smoking** had remarkable influence on the cholesterol concentration in the serum lipo-protein of healthy subjects. The levels of **HDL**-C **HDL**2-C, **HDL**3-C and **HDL**2-C/**HDL**3-C of the **smoking** group were obviously lower than those of the non-**smoking** group, while the levels of **LDL**-C, V**LDL**-C and **LDL**-C/**HDL**-C of the **smoking** group were obviously higher than those of the non-**smoking** group. Moreover, these indices were significantly associated with the **smoking** amount, **smoking** duration, depth of inhalation. **Smoking** was an important dangerous factor for lowering levels of **HDL**-C, **HDL**2-C, **HDL** 3-C, **HDL**2-C/**HDL**3-C and raising levels of **LDL**-C, V**LDL**-C, **LDL**-C/**HDL**-C. The relative risk (RR) of the two factors were estimated to be 1.09-5.77 and 2.37-3.57 respectively. The levels of the 7 indices such as **HDL**-C of passive smokers were identical with those of light smokers. This showed that passive **smoking** also had marked influence on cholesterol concentrations in serum lipoprotein.

144: Clin Investig 1992 Mar-Apr;70(3-4):263-8
Smoking influences the atherogenic potential of low-density lipoprotein.

Scheffler E, Wiest E, Woehrle J, Otto I, Schulz I, Huber L, Ziegler R, Dresel HA

Medizinische Klinik, Universitat Heidelberg.

The possible influence of **smoking** on the low-density lipoprotein (**LDL**) and its biological activity was investigated. Plasma **LDL** was prepared from healthy male smokers and nonsmokers, and oxidized with Cu (II) as prooxidant. Oxidized **LDL** from smokers generated significantly more lipid peroxidation products, so-called thiobarbituric acid reactive substances (**TBARS**), when compared to oxidized nonsmoker **LDL**. Analysis of vitamin E levels in **LDL** obtained from both smokers and nonsmokers revealed that the vitamin E content of smoker **LDL** was significantly less than that of nonsmoker **LDL**. The amounts of cholesteryl esters formed in cultured P388. D.1 macrophages were greater in the presence of smoker **LDL** than with nonsmoker **LDL**. The data suggest that some of the proatherogenic effects of **smoking** may be related to oxidative modification of **LDL** and alteration of its biological activity. PMID:

PM3000457419

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

145: Am J Epidemiol 1992 Feb 15;135(4):331-40

Smoking, lipids, glucose intolerance, and blood pressure as risk factors for peripheral atherosclerosis compared with ischemic heart disease in the Edinburgh Artery Study.

Fowkes FG, Housley E, Riemersma RA, Macintyre CC, Cawood EH, Prescott RJ, Ruckley CV

Department of Public Health Sciences, University of Edinburgh, United Kingdom.

The aim was to determine if certain risk factors in the general population are more strongly related to peripheral arterial disease than to ischemic heart disease. Arterial disease in the lower limbs was measured by means of the World Health Organization questionnaire on intermittent claudication, the ankle brachial pressure index, and a reactive hyperemia test in 1,592 men and women aged 55-74 years selected randomly in 1988 from the age-sex registers of 10 general practices in Edinburgh, Scotland. Peripheral arterial disease was strongly related to lifetime cigarette **smoking**, with additional risks in current and exsmokers of less than 5 years. Multiple regression of risk factors on measures of peripheral arterial disease showed associations with diabetes mellitus (but not impaired glucose tolerance), systolic blood pressure, and serum cholesterol; inverse association with high-density lipoprotein cholesterol; and only univariate association with triglycerides. In multiple logistic regressions of risk factors on six separate indicators of cardiovascular disease, the only consistent difference was that **smoking** increased the risk of peripheral arterial disease (range of odds ratios, 1.8-5.6) more than heart disease (range of odds ratios, 1.1-1.6). Diabetes mellitus was not a stronger risk factor for peripheral arterial disease.

PM3000457420

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

146: J Clin Epidemiol 1992 Jan;45(1):77-84

Gender differences in platelet count and its association with cigarette smoking in a large cohort in Israel.

Green MS, Peled I, Najenson T

Cardiovascular Epidemiology Unit, Loewenstein Hospital, Raanana, Israel.

Cigarette **smoking** has an effect on platelet function and aggregation although the sensitivity of platelet count in reflecting this phenomenon is not known. The association of platelet count with **smoking** habits was examined in a cohort of 5017 Israeli industrial workers aged 20-64 years. Males had a significantly lower age-adjusted mean platelet count than females (225,600 vs 247,800/microliters; p less than 0.001). Female smokers had lower platelet counts than non-smokers (231,000 for heavy vs 252,000 for never smokers) with a strong dose-response relationship (p less than 0.0001), whereas among males platelet count was slightly higher in smokers (224,000 for non-smokers vs 227,000 for heavy smokers; p = 0.243). The difference in platelet count between the sexes remained almost identical after controlling for **smoking** status and hematocrit. In multiple regression analysis, the negative association between **smoking** and platelet count in women remained highly significant (p less than 0.001) after controlling for ethnic origin, alcohol consumption, body mass, hematocrit, cholesterol and **HDL**-cholesterol, whereas for males the slight positive association was not significant. The reduced platelet count observed in males compared with females and in female smokers, suggests that platelet count may reflect sex differences in hemostasis and the effects of **smoking** on the hemostatic system. This may have implications for the mechanisms underlying the pathogenesis of ischemic heart disease and should be explored further.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

147: Arch Intern Med 1992 Jan;152(1):90-6

Gemfibrozil also corrects dyslipidemia in postmenopausal women and smokers.

Koskinen P, Kovanen PT, Tuomilehto J, Manninen V

Wihuri Research Institute, Helsinki, Finland.

We compared the efficacy of three formulations and two dosage regimens of gemfibrozil in 322 dyslipidemic (non-high-density lipoprotein [HDL] cholesterol level, greater than or equal to 5.2 mmol/L [greater than or equal to 200 mg/dL]) middle-aged male and postmenopausal female patients in a 1-year open-label trial. Of the patients studied, 109 received the standard 1200-mg dose of gemfibrozil, ie, two 300-mg capsules twice daily; 107 received one 600-mg tablet twice daily; and 106 received a single dose of 900 mg of gemfibrozil in two 450-mg tablets in the evening. The three treatment groups showed equal changes in each lipoprotein measure studied, ie, in serum levels of triglycerides, total cholesterol, low-density lipoprotein and HDL cholesterol, HDL subfractions HDL2 and HDL3, and apolipoproteins A-I, A-II, and B. When the therapeutic responses were analyzed separately in men (n = 219) and women (n = 103), significantly greater decreases in serum levels of total triglycerides, low-density lipoprotein cholesterol, and apolipoprotein B, and a significantly greater increase in HDL3 cholesterol level and apolipoprotein A-I/B ratio, were seen in the women. When the study population was divided into smokers (n = 80) and nonsmokers (n = 242), the changes were similar in all lipoprotein measures except HDL3 cholesterol level, in which a significantly greater increase was seen in the non-smokers. This study showed that gemfibrozil is as effective, or more so, in dyslipidemic postmenopausal women as in dyslipidemic middle-aged men, and that **smoking** does not abolish its lipid-regulating effects. Importantly, a daily dose of 900 mg was found to be as effective as the standard dose of 1200 mg.

Publication Types:
Clinical trial
Randomized controlled trial

PM3000457422

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

148: Atherosclerosis 1991 Oct;90(2-3):127-39
Published erratum appears in Atherosclerosis 1991 Dec;91(3):279

Fish oil ingestion in smokers and nonsmokers enhances peroxidation of plasma lipoproteins.

Harats D, Dabach Y, Hollander G, Ben-Naim M, Schwartz R, Berry EM, Stein O, Stein Y

Department of Medicine B, Lipid Research Laboratory, Hadassah University Hospital, Jerusalem, Israel.

The effect of fish oil ingestion (10 g MaxEPA/day) on the susceptibility of plasma lipoproteins to peroxidation was examined in 20 smokers (study A and B) and 22 nonsmokers (study C). The subjects were examined at the onset of each study (baseline values), divided into control and experimental groups and reexamined 4 weeks later. Smokers were examined 40 h after abstention from **smoking** (0 time) and 90 min after acute **smoking** (4-6 cigarettes). The parameters studied were **TBARS**, which provide an indication of peroxidative injury, and metabolism of conditioned **LDL** by macrophages as a biological indicator. These parameters were significantly higher (P less than 0.05-0.001) when the 90 min values of smokers were compared to time 0. After 4 weeks of fish oil ingestion, a significant rise above baseline values (33-50%) in plasma and **LDL TBARS** was found in smokers examined at time 0 and after acute **smoking**. Peroxidative modification of **LDL** isolated from smokers fed fish oil resulted in significantly higher **TBARS** (34-41%) and its metabolism by macrophages was higher (65-139%) compared to baseline values. In nonsmokers, the baseline values of the above parameters were lower than in smokers. Ingestion of fish oil resulted in a significant rise in **TBARS** in plasma (33%), **LDL** (137%), conditioned **LDL** (36-40%) and metabolism of conditioned **LDL** (70%) by macrophages. In 6 nonsmokers and 4 smokers, 400 mg of vitamin E/day were given with the fish oil. In the nonsmokers, vitamin E counteracted the effect of fish oil more effectively than in the smokers. In the light of the present results, indiscriminate recommendation of fish oil supplementation to the population at large should be cautioned.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

149: Am J Epidemiol 1991 Sep 15;134(6):583-9

Polyunsaturated fatty acids in adipose tissue in European men aged 38 years in relation to serum lipids, smoking habits, and fat distribution.

Seidell JC, Cigolini M, Deslypere JP, Charzewska J, Ellsinger BM

Department of Human Nutrition, Wageningen University, The Netherlands.

Fat biopsies were taken from 327 men aged 38 years from five different European communities in 1988-1989. Linoleic acid content varied widely (F = 110.6, p less than 0.001) and was lowest in men from Poland (8.6%) and highest in men from Belgium (16.7%). Adipose tissue content of alpha-linolenic acid was subject to less variation (F = 13.9, p less than 0.001) and was lowest in men from Italy (0.5%) and highest in men from Sweden and the Netherlands (0.9%). In analysis combining information from all centers, linoleic acid was negatively correlated to low density lipoprotein cholesterol (r = -0.15, p less than 0.01) and total cholesterol (r = -0.17, p less than 0.01). alpha-Linolenic acid was negatively correlated to serum triglycerides only (r = -0.14, p less than 0.05). These fatty acids were not related to body mass index, waist/hip ratio, or **smoking** habits. The authors conclude that there are major differences in the fatty acid composition of adipose tissue in different European populations but that these do not explain the significant differences in serum high density lipoprotein cholesterol and serum triglycerides among the different populations.

PM3000457424

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

150: Prev Med 1991 Sep;20(5):655-9

Association between baseline risk factors, cigarette smoking, and CHD mortality after 10.5 years. MRFIT Research Group.

Shaten BJ, Kuller LH, Neaton JD

Division of Biostatistics, School of Public Health, University of Minnesota, Minneapolis 55414-3080.

METHODS. The association between baseline risk factors and death from coronary heart disease (CHD) after 10.5 years was investigated for cigarette smokers and nonsmokers who entered the Multiple Risk Factor Intervention Trial (MRFIT). RESULTS. Rates per thousand person-years of CHD mortality were higher for smokers than for nonsmokers at every level of baseline risk factors examined. There were significant associations between CHD mortality and plasma low-density lipoprotein and high-density lipoprotein cholesterol for smokers and nonsmokers. The inverse association between CHD mortality and high-density lipoprotein cholesterol was significantly stronger among nonsmokers compared with that among smokers and was attributable to a very strong association for former smokers. An inverse relationship between CHD and body mass index was evident for smokers and nonsmokers. Rates of CHD death rose sharply when levels of fasting glucose exceeded 140 mg/dl, and there was a significant association between CHD mortality and blood sugar levels for nonsmokers but not for smokers. For both smokers and nonsmokers, an inverse univariate association between alcohol consumption and CHD mortality was evident. This association, however, did not persist after adjustment for plasma high-density lipoprotein cholesterol. CONCLUSION. Intervention on blood pressure and blood lipids is particularly important among cigarette smokers because of their increased risk of CHD death. The different associations between high-density lipoprotein cholesterol, fasting serum glucose, and CHD mortality for smokers and nonsmokers requires further investigation.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

151: Sangyo Igaku 1991 Jul;33(4):231-40

An evaluation of efficacy of cigarette smoking cessation in preventing low levels of serum high-density lipoprotein (HDL) cholesterol.

Nishihara H, Takashima Y, Watanabe G, Kondo H

Osaka Health Center, Mitsui Taiyo Kobe Bank, Limited.

Correlation of serum high-density lipoprotein cholesterol (**HDL**-C) with cigarette **smoking** and alcohol consumption habit was investigated in 562 male office workers aged 31 to 60 yr. **HDL**-C concentrations were found to be positively associated with alcohol consumption in subjects with relative weight below 10%, but a positive association was not observed in obese subjects having relative weight of 10% or above. In contrast, **HDL**-C levels were significantly lower in smokers than in non-smokers regardless of obesity. The effectiveness of **smoking** cessation in preventing low levels of serum **HDL**-C was estimated by comparing prevalence rates of **HDL**-C levels lower than an arbitrarily determined **HDL**-C cutoff value in smokers with those in non-smokers. The estimation was made with unadjusted subjects and also with subjects adjusted for age, relative weight and alcohol consumption. The effectiveness was found to be considerably high in heavy smokers having lower **HDL**-C levels (less than or equal to 35 mg/dl) with or without hypercholesterolemia (greater than or equal to 220 mg/dl) and further remarkably high in all smokers having hypertriglyceridemia (greater than or equal to 300 mg/dl) besides lower **HDL**-C levels. It is therefore expected that health education focused on stopping **smoking** can produce favorable alterations in **HDL**-C for preventing coronary heart disease, especially in heavy smokers having low serum **HDL**-C levels concomitant with hypercholesterolemia and/or hypertriglyceridemia.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

152: Clin Sci (Colch) 1991 Jul;81(1):11-5
Cigarette smoking and urinary excretion of markers for platelet/vessel wall interaction in healthy women.

Rangemark C, Wennmalm A

Department of Clinical Physiology, Gothenburg University, Sweden.

1. Cigarette **smoking** is known to increase the risk of cardiovascular disease in both men and women. Experimental and epidemiological studies have demonstrated that cigarette **smoking** is associated with several indices of increased platelet activation and platelet/vessel wall interaction in men. The aim of the present study was to test the hypothesis that cigarette **smoking** is linked to an increased platelet activity in women also. 2. In 26 healthy **smoking** and non-**smoking** women (age 21-49 years) the urinary excretion of the thromboxane A2 metabolite 2,3-dinor-thromboxane B2 (an index of platelet activation) and of the prostacyclin metabolite 2,3-dinor-6-keto-prostaglandin F1 alpha (an index of platelet/vessel wall interaction) were analysed by g.c.-m.s. in samples collected on days 3, 10 and 20 of their respective menstrual cycles. 3. The urinary excretion of 2,3-dinor-thromboxane B2 did not vary significantly during the menstrual cycle, either in the smokers or in the non-smokers. It was consistently higher (P less than 0.004) in the group of smokers (average of day 3, 10 and 20, 395 +/- 61 pg/mg of creatinine; mean +/- SEM) than in the group of non-smokers (average 188 +/- 22 pg/mg of creatinine). 4. The urinary excretion of 2,3-dinor-6-keto-prostaglandin F1 alpha did not differ between the groups on any of the days studied (average on days 3, 10 and 20 in the smokers and non-smokers was 281 +/- 50 and 227 +/- 30 pg/mg of creatinine, respectively.(ABSTRACT TRUNCATED AT 250 WORDS)

153: Nippon Eiseigaku Zasshi 1991 Jun;46(2):699-708
The effects of drinking, smoking and physical constitution on high density lipoprotein cholesterol, apolipoprotein AI and AII levels.

Maeda K, Hashimoto S, Okamoto K, Saito Y, Ohtsuka T, Ohtsuka S, Takahashi A, Okamoto N, Ohno K, Hattori Y, et al

Department of Public Health, Aichi Medical University.

PM3000457427

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

154: Circulation 1991 May;83(5):1698-704

Relation between tobacco use and urinary excretion of thromboxane A2 and prostacyclin metabolites in young men.

Wennmalm A, Benthin G, Granstrom EF, Persson L, Petersson AS, Winell S
Department of Clinical Physiology, Gothenburg University, Sweden.

BACKGROUND. Cigarette **smoking** is a risk factor for cardiovascular disease. The present study addressed the effect of tobacco use on the formation of two eicosanoids, thromboxane A2 and prostacyclin, which have been implicated in both acute and chronic cardiovascular disorders. METHODS AND RESULTS. In 577 randomly sampled 18-19-year-old men, the urinary excretion of the 2,3-dinor metabolites of thromboxane A2 and prostacyclin (Tx-M and PGI-M, respectively) was analyzed and related to the subjects' self-reported use of tobacco. Sixty-five percent of the subjects used no tobacco, 7.5% were cigarette smokers, 22% used wet (oral) snuff, and the rest reported a mixed use of tobacco. The urinary excretion of Tx-M was higher (p less than 0.001) in cigarette smokers than in those not using tobacco (180 versus 128 pg/mg creatinine) and was correlated (r = 0.35, p less than 0.05) with the daily cigarette consumption. Snuff users had no increase in their urinary excretion of Tx-M, despite urinary cotinine levels comparable to those in the cigarette smokers (1,210 and 1,560 ng/ml, respectively). The excretion of PGI-M did not differ between non-tobacco users, cigarette smokers, and snuff users. CONCLUSIONS. We conclude that cigarette **smoking**, but not the use of snuff, facilitates the formation of thromboxane A2. We propose that such an increased formation reflects platelet activation in the absence of vascular injury and that it may be of significance for the subsequent development of cardiovascular disease.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

155: Am J Cardiol 1991 May 1;67(11):987-92
Dyslipidemic effects of cigarette smoking on beta-blocker-induced serum lipid changes in systemic hypertension.

Vyssoulis GP, Karpanou EA, Pitsavos CE, Toutouza MA, Paleologos AA, Toutouzas
Department of Cardiology, University of Athens, Greece.

To assess the effects of beta blockers on lipids and apolipoproteins in cigarette smokers and nonsmokers, 330 patients with systemic hypertension received 1 month of placebo and 6 months of beta-blocker monotherapy. Serum total cholesterol, triglycerides, high-density lipoprotein (**HDL**) cholesterol, low-density lipoprotein (**LDL**) cholesterol, and apolipoproteins A1 and B were measured. Total cholesterol increased with propranolol (smokers vs nonsmokers, 8 vs 2%); increased for smokers and decreased for nonsmokers with atenolol (8 vs -3%), metoprolol (6 vs -1%) and pindolol (7 vs -6%); and decreased for both groups with celiprolol (-3 vs -10%). **HDL** cholesterol decreased with propranolol (smokers vs nonsmokers, -8 vs -18%), atenolol (-7 vs -2%) and metoprolol (-12 vs -1%); increased for smokers and decreased for nonsmokers with pindolol (11 vs -2%); and increased for both groups with celiprolol (5 vs 6%). Similar trends were observed with **LDL** cholesterol and the total/**HDL** cholesterol ratio. It is concluded that early noncardioselective beta blockers such as propranolol have significant dyslipidemic effects in both smokers and nonsmokers. Cardioselective drugs such as atenolol and metoprolol, or drugs with partial agonist activity such as pindolol, have variable effects. Celiprolol, a new, highly cardioselective beta 1 blocker with partial beta 2 agonist activity and vasodilatory properties, has favorable effects on lipids and minimizes the dyslipidemic effects associated with **smoking**.

Clinical trial
Randomized controlled trial

156: Indian J Physiol Pharmacol 1991 Apr;35(2):138-40
Blood cholesterol and HDL cholesterol in cigarette smokers.

Pugalendi KV, Ramakrishnan S

Department of Biochemistry, Rajah Muthiah Medical College, Annamalai University,Tamil Nadu.

24 cigarette smokers were investigated for their blood cholesterol and **HDL** cholesterol. They had elevated total cholesterol compared to age and sex matched controls. 21 smokers out of 24 had significant decrease of **HDL** cholesterol. It is suggested that **smoking**, which is a major risk factor for coronary heart disease, might act through its effect on total cholesterol and **HDL** cholesterol.

PM3000457429

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

157: Pathology 1991 Apr;23(2):98-102
Effect of smoking cessation on serum apolipoprotein A-I and A-II concentrations.

Masarei JR, Puddey IB, Vandongen R, Beilin LJ, Lynch WJ

Department of Medicine, University of Western Australia, Perth.

This study investigated the effects of 6 weeks' **smoking** cessation on serum levels of total-cholesterol, triglyceride, high-density lipoprotein cholesterol (**HDL**-C) and apolipoproteins A-I and A-II (apo A-I and apo A-II) in 64 subjects of both sexes. **Smoking** cessation was associated with an increase in levels of apo A-II. Concurrent changes in weight and alcohol consumption during attempted **smoking** cessation, together with change in thiocyanate level, were entered as predictor variables into a multiple regression analysis. The change in apo A-II was found to be best accounted for by change in plasma thiocyanate level, and, in women, change in **HDL**-C and apo A-I by change in weight. The changes induced by **smoking** cessation may be due, at least in part, to associated changes in alcohol consumption and/or dietary intake, but in the case of apo A-II there is evidence of a more direct effect.

158: Thromb Haemost 1991 Mar 4;65(3):317-9
Platelets of habitual smokers have reduced susceptibility to aggregating agent.

Foo LC, Roshidah I, Aimy MB

Institute for Medical Research, Kuala Lumpur, Malaysia.

Platelet aggregation to collagen, and productions of 6-keto-prostaglandin-F1-alpha and thromboxane B2 during aggregation were measured after an overnight fast, involving both food and cigarettes, in 19 clinically healthy habitual smokers (10 or more cigarettes/day) and 23 non-smokers receiving the same diet. The subjects (all males; ages = 21-30 years) were residents of a school hostel. Mean platelet aggregation was significantly lower in smokers than non-smokers (23.2 ohms vs 31.5 ohms, p less than 0.005). Non-smokers had significantly higher mean concentration of 6-keto-prostaglandin-F1-alpha than smokers (109.8 pmol/l vs 92.3 pmol/l, p less than 0.05). The level of thromboxane B2 did not differ significantly between the two groups. These observations suggest that the role of **smoking** as a risk factor for ischaemic heart disease is unlikely to be related to a direct enhancement of aggregation. On the contrary, the observations seem to suggest that habitual **smoking** may directly reduce platelet aggregability.
Comments:
Comment in: Thromb Haemost 1991 Dec 2;66(6):739-40

159: Mayo Clin Proc 1991 Mar;66(3):259-67
Serum lipids and lipoproteins are less powerful predictors of extracranial carotid artery atherosclerosis than are cigarette smoking and hypertension.

Homer D, Ingall TJ, Baker HL Jr, O'Fallon WM, Kottke BA, Whisnant JP

PM3000457430

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

Department of Neurology, Mayo Clinic, Rochester, MN 55905.

The effect of serum lipids and lipoproteins on extracranial carotid artery atherosclerosis (CAS) was studied in patients who underwent carotid arteriography. Serum lipid and lipoprotein values along with data on other potential predictors of extracranial CAS were determined in 240 patients who had at least one extracranial carotid artery visualized. In a multiple logistic regression analysis, the independently significant predictors of the presence of extracranial CAS were, in decreasing order of significance, duration of **smoking** of cigarettes, hypertension, age, and low-density lipoprotein cholesterol. Serum cholesterol, triglycerides, high-density lipoprotein cholesterol, and apolipoprotein A-I did not show an independent effect. Although low-density lipoprotein cholesterol was an independent predictor of the presence of extracranial CAS, its effect as a predictor was far outweighed by the effects of the duration of **smoking** of cigarettes and a history of hypertension.

Comments:
Comment in: Mayo Clin Proc 1991 Mar;66(3):327-31
Comment in: Mayo Clin Proc 1992 Mar;67(3):303-4

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

160: Z Gerontol 1991 Mar-Apr;24(2):76-80
Effect of smoking on different biological parameters in aging mice.

Boross M, Penzes L, Izsak J, Rajczy K, Beregi E
Gerontology Center, Semmelweis Medical University, Budapest, Hungary.

To investigate the harmful effect of **smoking** three groups of CBA/Ca male mice of different ages were subjected to **smoking** for different time durations. Body weight changes and acute cold tolerance were measured throughout the experiment. Thyroid hormone levels (T4, T3), TSH and lipid peroxidation products (as **malondialdehyde** and lipofuscin) were determined from either the blood or some organs. There was a decrease in body weight related to aging and it was most pronounced in the oldest animals (Group III). However, significant body-weight loss due to **smoking** was found in the youngest animals (Group I). Similarly, **smoking** resulted in a body-weight loss of the other two older groups (Groups II and III) as well. The greatest change in withstanding cold stress was measured in Group I and less so in Group II, as a consequence of **smoking**. Simultaneously, the youngest animals (Group I) showed the most remarkable changes in thyroxine (T4) and 3,3,4-triiodothyronine (T3) serum concentrations. Both hormone levels were significantly lower in the smokers. The T3 serum levels of the oldest animals (Group III) did not differ, while the T4 levels apparently increased. The TSH blood level in the oldest group was lower (by 20%) in the smokers compared to controls. **Malondialdehyde** (MDA) and lipofuscin content in most of the organs were considerably higher in the aging animals than those of the younger ones. The most significant elevations of these lipid peroxidation products were found in the smokers compared to the age-matched controls. The present results indicate that **smoking** probably accelerates the aging process.

161: Int J Exp Pathol 1991 Feb;72(1):1-7
Increased production of oxygen free radicals in cigarette smokers.
Kalra J, Chaudhary AK, Prasad K

Department of Pathology, College of Medicine, University of Saskatchewan,

Oxygen free radicals are known to produce damage in many biological tissues. Cigarette **smoking** is a major risk factor for various diseases. It is possible that oxygen free radical producing activity of polymorphonuclear (PMN) leucocytes is increased by cigarette **smoking**. We studied the oxygen free radical producing (luminol-dependent chemiluminescent) activity of PMN leucocytes in blood and the **malondialdehyde** (lipid peroxidation product) content of blood and serum in nonsmokers and smokers. The zymosan-induced chemiluminescent activity was measured on a LKB 1251 luminometer. The **malondialdehyde** (MDA) was measured as thiobarbituric acid (TBA) reactive substances. The chemiluminescent activity due to oxygen-derived free radicals (superoxide anion, hydrogen peroxide, hydroxyl radical) and superoxide dismutase (SOD)-inhibitable (superoxide anion) in nonsmokers were 1215.1 +/- 91.1 and 849.3 +/- 72.3 mV min/10(6) PMN leucocytes respectively. There was a significant increase in the oxygen-derived free radicals and SOD-inhibitable chemiluminescence in smokers. The values of blood and serum MDA were 171.7 +/- 6.1 and 222.2 +/- 5.6 nmoles/l respectively in nonsmokers. There was an increase in both blood and serum MDA in smokers. These results suggest that the increased generation of oxygen free radicals by PMN leucocytes might be responsible for an enhanced risk of various diseases related to cigarette **smoking**.

PM3000457432

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

162: Adv Prostaglandin Thromboxane Leukot Res 1991;21B:777-9
Effect of smoking on prostaglandin, thromboxane and leukotriene synthesis by human gastric mucosa.

Hudson N, Daneshmend TK, Hurst S, Bhaskar NK, Brown NS, Hawkey CJ

Department of Therapeutics, University Hospital, Nottingham, United Kingdom.

163: Sov Med 1991;(9):46-9
[Characteristics of the indicators of the lipoprotein spectrum of blood and the main risk factors of the development of arteriosclerosis among university students in different regions of the USSR].
[Article in Russian]

Olfer'ev AM, Shamarin VM, Petrosian KIu, Koval' SN, Konobeevskaia IN, Aripov BS, Zadoia NA, Nazarenko IL, Kanskaia NV, Kulikov SM

164: JAMA 1990 Dec 19;264(23):3018-24

Relationship of atherosclerosis in young men to serum lipoprotein cholesterol concentrations and smoking. A preliminary report from the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group.

Investigators in eight communities collected aortas, right coronary arteries, blood, and associated information from 390 males, 15 to 34 years of age, who died of violent causes. Pathologists at central laboratories graded the arteries for atherosclerotic lesions, and serum lipoprotein cholesterol and thiocyanate concentrations were measured. The percentage of intimal surface involved with atherosclerotic lesions in both the aorta and the right coronary artery was positively associated with serum very low-density lipoprotein + low-density lipoprotein cholesterol concentration and negatively associated with serum high-density lipoprotein cholesterol concentration. The serum thiocyanate concentration, a marker for **smoking**, was strongly associated with prevalence of raised lesions, particularly in the abdominal aorta. The effect of **smoking** was not explained by lipoprotein levels. Blacks had more extensive total surface involvement of the aorta after adjustment for lipoprotein cholesterol levels and **smoking**. These associations indicate that serum lipoprotein cholesterol concentrations and **smoking** are important determinants of the early stages of atherosclerosis in adolescents and young adults.
Publication Types:

Clinical trial
Multicenter study
Comments:
Comment in: JAMA 1990 Dec 19;264(23):3060-1

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

165: Int J Epidemiol 1990 Dec;19(4):911-7

Association of serum low density lipoprotein cholesterol, smoking and hypertension with different manifestations of atherosclerosis.

Salonen JT, Salonen R

Department of Community Health and General Practice, University of Kuopio, Finland.

We investigated the association of elevated serum low density lipoprotein (**LDL**) cholesterol levels, **smoking** and hypertension with different manifestations of carotid atherosclerosis in a population-based sample of 720 Eastern Finnish men aged 42, 48, 54 or 60 years, examined in the Kuopio Ischaemic Heart Disease Risk Factor Study. Carotid atherosclerosis was assessed with high-resolution B-mode ultrasonography. Men who had neither a history nor symptoms of cardiovascular disease with serum **LDL** cholesterol concentration in the highest tertile (4.17 mM or more) had 3.40-fold (95% confidence interval (CI) 1.98-5.84) age-, **smoking**- and hypertension-adjusted probability of intimal-medial thickening as compared to men in the lowest serum **LDL** cholesterol tertile. The odds ratio for carotid plaque versus intimal-medial thickening was only 1.03 (95% CI 0.47-2.28). The respective odds ratios for **smoking** (28 pack-years or more) were 1.62 (95% CI 0.79-3.32) and 3.02 (95% CI 1.41-6.47) and those for hypertension were 1.10 (95% CI 0.70-1.73) and 0.99 (95% CI 0.53-1.84). Our findings suggest that elevated serum **LDL** cholesterol concentration associates with an increased risk of common carotid arterial wall thickening, whereas **smoking** is associated more strongly with carotid plaques than intimal-medial thickening. Our cross-sectional data do not support association between hypertension and either manifestation of carotid atherosclerosis.

PM3000457434

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

166: Int J Epidemiol 1990 Dec;19(4):881-8

The relationship of white blood cell count to other cardiovascular risk factors.

Hansen LK, Grimm RH Jr, Neaton JD

Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis 55414.

Baseline data for the 12,866 men from the Multiple Risk Factor Intervention Trial was used to study factors related to white blood cell (WBC) count. White blood cell count was significantly higher in smokers (7853 cells/mm3) and ex-smokers (7091 cells/mm3) who stopped **smoking** less than one year before than in ex-smokers who stopped more than one year before (6255 cells/mm3) and those who never smoked (6094 cells/mm3). In current cigarette smokers, white blood cell count was significantly related to number of cigarettes smoked, degree of inhalation, and duration of **smoking** (p less than 0.001 for each). In addition, white blood cell count was higher in non-cigarette smokers who smoked pipes, cigars, or cigarillos than among men who did not smoke tobacco (p less than 0.001). White blood cell count was lower in blacks (by 877 cells/mm3) and Orientals (by 634 cells/mm3) than in whites. Leukocyte count also showed a strong inverse association with high density lipoprotein (**HDL**)-cholesterol, a positive association with triglycerides independent of cigarette use, and a positive association with low density lipoprotein (**LDL**)-cholesterol in smokers only. Leukocyte counts were inversely related to total family income and alcohol consumption. We conclude that elevated leukocyte count is independently associated with other risk factors for coronary heart disease (CHD) such as amount and duration of **smoking** as well as an atherogenic profile, and these relationships should be considered when using white blood cell count as a predictor of coronary heart disease.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

167: Am J Med 1990 Dec;89(6):761-71

Cigarette smoking, adiposity, non-insulin-dependent diabetes, and coronary heart disease in Japanese-American men.

Fujimoto WY, Leonetti DL, Bergstrom RW, Shuman WP, Wahl PW
Department of Medicine, University of Washington, Seattle 98195.

PURPOSE: Coronary heart disease has been described to be increased with both glucose intolerance and cigarette **smoking**. All three of these have also been reported to be associated with central adiposity (disproportionate deposition of fat on the trunk compared to the extremities). The purpose of this analysis was to determine the relationship of cigarette **smoking** to glucose intolerance and coronary heart disease, the relationship of cigarette **smoking** to risk factors such as adiposity, body fat distribution, and plasma lipoprotein and insulin levels, the relationship of cigarette **smoking** to these risk factors independent of disease status, and whether these risk factors could account for any of the relationship between cigarette **smoking** and disease status. PATIENTS AND METHODS: The study design was cross-sectional. The study sample contained 219 middle-aged and elderly Japanese-American men: 77 with normal and 74 with impaired glucose tolerance and 68 with type II diabetes. There were 54 men with coronary heart disease. A detailed **smoking** history was obtained. Glucose tolerance status was established by medical history and a 75-g oral glucose tolerance test. Coronary heart disease was determined by medical history and a resting electrocardiogram. Adiposity and fat distribution measurements were body mass index (kg/m2), skinfold thicknesses, body circumferences, and cross-sectional fat areas by computed tomography. Levels of insulin, C-peptide, cholesterol (total, low-density lipoprotein [**LDL**], high-density lipoprotein [**HDL**], **HDL**2, **HDL**3, very-low-density lipoprotein [**VLDL**]), and triglyceride (total, **VLDL**) were measured in fasting blood specimens. RESULTS: A central pattern of body fat was associated with both non-insulin-dependent diabetes mellitus and coronary heart disease. **Smoking** history was related to both adiposity and body fat distribution, and was strongly related to coronary heart disease but not to diabetes. Past smokers who had smoked up to a month ago were the heaviest while present smokers who were currently **smoking** or had smoked within the past month were the leanest. However, although present smokers had reduced amounts of fat, this was attributable to those present smokers without heart disease. Present smokers with heart disease were not as lean and had increased amounts of intra-abdominal fat. Past smokers had the greatest amount of central fat and this was attributable to those with heart disease. By two-way (**smoking** history and coronary heart disease status) analysis of covariance, **smoking** history was significantly related only to subcutaneous fat disposition on the chest and abdomen independent of coronary heart disease, while coronary heart disease status was strongly related to plasma levels of insulin C-peptide, **VLDL**, **HDL**, **HDL**2, and **HDL**3 cholesterol, and total and **VLDL** triglyceride, independent of **smoking** history. Further analysis showed that none of the body fat variables could account for the risk of coronary heart disease associated with **smoking** history. Higher fasting plasma C-peptide levels in past smokers accounted statistically for part of the risk of coronary heart disease associated with cigarette **smoking**. However, this effect was not mediated by any of the body fat measurements. CONCLUSIONS: Disproportionately increased intra-abdominal fat is related to coronary heart disease but not to **smoking** history. **Smoking** history is related to coronary heart disease but not to diabetes. Weight gain is associated with **smoking** cessation and appears to be concentrated in the central subcutaneous regions, especially for those who have coronary heart disease. Weight gain associated with cessation of **smoking** appears to be unrelated to atherogenic

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

changes in lipids, lipoproteins, or insulin. Other pathogenic processes must be considered in the association between **smoking** and coronary heart disease.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

168: Atherosclerosis 1990 Nov;85(1):47-54

Effect of vitamin C and E supplementation on susceptibility of plasma lipoproteins to peroxidation induced by acute smoking.

Harats D, Ben-Naim M, Dabach Y, Hollander G, Havivi E, Stein O, Stein Y

Department of Medicine B, Hadassah University Hospital, Jerusalem, Israel.

The effect of acute **smoking** on plasma lipoproteins was studied in seventeen smokers. In study 1, 7 subjects were examined prior to and 2 weeks after supplementation with vitamin C. In study 2, the effect of acute **smoking** was first determined in 10 additional subjects and subsequently they were divided into 3 groups, 3 and 4 subjects were supplemented with vitamin C or E, respectively, for 4 weeks, and 3 remained untreated. Plasma and **LDL TBARS** were examined at time zero (i.e., 40-48 h after total abstention from **smoking**) and at 90 min after acute **smoking** (5-7 cigarettes). In all 17 subjects examined prior to vitamin supplementation, significantly higher **TBARS** values were found in plasma, native **LDL** and **LDL** conditioned with smooth muscle cells (SMC) when the 90 min values were compared to 0 time. The **LDL** isolated after 90 min and conditioned with SMC was metabolized more extensively by mouse peritoneal macrophages than its zero time counterpart. The differences between the 0 time and 90 min values were not seen after the subjects had been supplemented with vitamin C for 2 or 4 weeks or with vitamin E for 4 weeks. The present results indicate that acute **smoking** exerts an oxidative stress on plasma lipoproteins and that higher plasma levels of natural antioxidants, such as vitamins C and E have a protective role.

PM3000457438

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

169: Atherosclerosis 1990 Oct;84(2-3):239-44

Influence of smoking, body fat distribution, and alcohol consumption on serum lipids, lipoproteins, and apolipoproteins in early postmenopausal women.

Haarbo J, Hassager C, Schlemmer A, Christiansen C

Department of Clinical Chemistry, Glostrup Hospital, University of Copenhagen, Denmark.

The impact of **smoking**, alcohol consumption, obesity, and body fat distribution (measured either directly by dual photon absorptiometry as abdominal fat% (AF%) or as the waist-to-hip ratio (WTH) on serum lipids, lipoproteins, and apolipoproteins was investigated in 148 early postmenopausal women. All the women were healthy and none were taking medication known to influence the parameters studied. Smokers had significantly higher levels of triglycerides, low density lipoprotein cholesterol (**LDL**-C), and apolipoprotein B (P less than 0.05), and higher ratios of **LDL**-C/**HDL**-C and apolipoprotein B/A-I (P less than 0.01), but lower levels of high density lipoprotein cholesterol (**HDL**-C) and apolipoprotein A-I (P less than 0.01). Moderate alcohol consumption was positively associated with **HDL**-C and apolipoprotein A-I (P less than 0.001). Body weight and body mass index (BMI) tended to be positively associated with an atherogenic lipoprotein and apolipoprotein profile. However, body fat distribution parameters (AF% and WTH) were stronger predictors of lipoproteins and apolipoproteins than were body weight and BMI, which did not seem to be independent predictors of lipoproteins and apolipoproteins. We conclude that cigarette **smoking** and a central fat distribution have a significant, independent, negative influence on lipids, lipoproteins, and apolipoproteins, whereas moderate alcohol consumption has a positive effect on these parameters in early postmenopausal women.

PM3000457439

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

170: Chest 1990 Oct;98(4):930-5

Pulmonary lipid peroxidation in cigarette smokers and lung cancer patients.

Petruzzelli S, Hietanen E, Bartsch H, Camus AM, Mussi A, Angeletti CA, Saracci R, Giuntini C

CNR Institute of Clinical Physiology, University of Pisa, Italy.

Lipid peroxidation (LPO) was studied in lung tissues of patients with lung cancer (LC, n = 37) or nonlung cancer (NLC, n = 13) and its relationships with the **smoking** habits and the degree of airway obstruction were investigated. Specimens of peripheral lung parenchyma, free of tumor tissue, were taken and the **malondialdehyde** (MDA) content was measured in the S-12 fractions. Airway obstruction was assessed by flow-volume curves, and data were expressed as percentage of the predicted values. Cigarettes smoked were expressed as pack-years. The patients with LC and NLC did not differ by MDA content, age, and number of pack-years. On the contrary, FEF75-85 and MEF75 were significantly lower in LC than in NLC patients (p less than 0.05). The MDA content was inversely correlated to number of days patients had refrained from **smoking** (r = -0.66, p less than 0.001). The MDA content was higher in recent smokers (ie, people **smoking** during the last 30 days before surgery) than in the other patients (0.136 +/- 0.007 vs 0.116 +/- 0.007 mumol/g of tissue, p less than 0.05) and, by considering only recent smokers, MDA content was higher in LC patients (0.144 +/- 0.008 mumol/g of tissue) than in NLC patients (0.113 +/- 0.014 mmol/g tissue, p = 0.059). When patients were divided into "high MDA" and "low MDA" groups, MEF75 was much lower in the high MDA group (35.1 +/- 3.4 percent) than in the low MDA group (55.1 +/- 8.1 percent) (p less than 0.01). These results suggest the following: (1) enhanced level of prooxidant state in the lungs is associated with recent cigarette **smoking**; (2) LC patients may be more prone than respective NLC patients to oxidative stress; (3) MDA level and degree of small airway obstruction were associated and differed between LC and NLC patients even though these groups did not differ in the percentage of recent smokers; and (4) a common free-radical mediated pathway may be active for both LC and small airway obstruction.

Comments:

Comment in: Chest 1992 Jan;101(1):290

PM3000457440

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

171: Eur Respir J 1990 Sep;3(8):872-9

Effects of nonsteroidal anti-inflammatory drugs on the bronchial hyperresponsiveness of middle-aged male smokers.

Lim TK, Turner NC, Watson A, Joyce H, Fuller RW, Pride NB

Dept of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London, UK.

Bronchial hyperresponsiveness (BHR) in smokers is believed to be a consequence of airway wall inflammation. We have examined the effects of treatment with nonsteroidal anti-inflammatory drugs (NSAID) on BHR to inhaled histamine, measured as the provocative concentration reducing forced expiratory volume in one second (FEV1) by 20% (PC20), in middle-aged male cigarette smokers in two separate double-blind, placebo-controlled, cross-over trials. Baseline FEV1 in these smokers ranged from 41-117% predicted values. In the first study 15 men (mean age 58 yrs, FEV1 2.20 l) were examined before and one hour after a single dose of 1.2 g aspirin. There was no significant change in PC20 (geometric mean 1.88 mg.ml-1 pre-aspirin, 1.89 mg.ml-1 post-aspirin) or baseline FEV1 and we observed no tachyphylaxis to the effects of inhaled histamine at one hour after placebo. In the second study 10 men (mean age 60 yrs, FEV1 2.53 l) were examined before and after three days' treatment with the NSAID flurbiprofen 50 mg t.d.s. Baseline PC20 was higher in this group than in the first study. There was no relationship between the excretion of urinary thromboxane metabolites and the intensity of BHR under baseline conditions; flurbiprofen greatly reduced the urinary excretion of thromboxane metabolites, but baseline FEV1 was not altered. Analysis of change in PC20 was complicated by a difference in baseline PC20 before the two treatments, but treatment with flurbiprofen did not significantly attenuate BHR. The results suggest that thromboxane or other cyclo-oxygenase products of arachidonic acid metabolism do not play an important role in the short-term maintenance of BHR to histamine in middle-aged male cigarette smokers.

Publication Types:
Clinical trial
Controlled clinical trial

PM3000457441

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

172: Rev Esp Cardiol 1990 Aug-Sep;43(7):432-7
[The Fuenlabrada's study: tobacco as cardiovascular risk factor in children and adolescents].

[Article in Spanish]

Plaza I, Mariscal RP, Ros-Jellici J, Munoz MT, Carratala J, Otero J, Madero R, Lopez D, Hidalgo I, Cobaleda A, et al

Hospitales Nino Jesus y La Paz. Universidad Autonoma de Madrid.

Smoking habits were studied in 1,274 healthy adolescents of both sexes, aged 10 to 18 years, of Fuenlabrada, Madrid. It was known by personal interview. 30% of the population were smokers. **Smoking** habits increased with age up to 18 years when 63% of males and 53% of females were smokers. **Smoking** prevalence was significantly higher among males than in females. Males and females smokers had significantly lower levels of C-**HDL** and higher levels of C-**LDL**/C-**HDL** ratio than non smokers. No differences were observed for anthropometric variables, body mass index, blood pressure, skin-fold thickness, total cholesterol, glucemia and uric acid. The implications of these findings are of concern in light of the apparently protective role of C-**HDL** in coronary heart disease. These findings provide valuable information to the promotion of anti**smoking** campaigns in adolescent age.

173: J Nutr Sci Vitaminol (Tokyo) 1990 Aug;36(4):377-85
Relationship between total cholesterol and high-density lipoprotein cholesterol and the effects of physical exercise, alcohol consumption, cigarette smoking and body mass index.

Koyama H, Ogawa M, Suzuki S

Department of Environmental Health Sciences, Tohoku University School of Medicine, Sendai, Japan.

Despite the fact that high-density lipoprotein cholesterol (**HDL**C) is a part of total cholesterol (TC), the serum level of this portion has been reported to have no or only a weak relationship to the TC level. The present study assessed the relationship between **HDL**C and TC considering alcohol consumption, cigarette **smoking**, and body mass index (BMI) in 366 male workers classified into three groups by the habitual physical exercise. The results showed the different effects of alcohol consumption, cigarette **smoking**, and BMI on the level of **HDL**C among these three groups, and alcohol consumption lowered the **LDL**C level only in the exercise group. The closest relationship between **HDL**C and TC was seen in the exercise group, even after taking other factors into account. The result suggests that the **HDL**C level must be evaluated relative to the level of TC. As an indicator of serum lipid patterns the validity of the ratio of **HDL**C to TC (**HDL**C/TC) was discussed.

PM3000457442

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

174: J Intern Med 1990 Jul;228(1):17-22
Eighty-year-old men without cardiovascular disease in the community of Malmo. Part II. Smoking characteristics and ultrasound findings, with special reference to glutathione transferase and pyridoxal-5-phosphate.

Pessah-Rasmussen H, Jerntorp P, Stavenow L, Elmstahl S, Hansen F, Seidegard J, Galvard H, Brattstrom L, Hamfelt A

Department of Medicine, Malmo General Hospital, Sweden.

A total of 1280 80-year-old men in the community of Malmo were questioned about **smoking** habits and the occurrence of cardiovascular disease (CVD). After a careful medical and duplex ultrasound examination, four groups were selected for further studies: (1) no CVD, non-smokers: (2) no CVD, smokers: (3) CVD, smokers: (4) CVD, non-smokers. In total 122 individuals participated. The average tobacco consumption by smokers was 13 g d-1 for 59 years. In the CVD group 45% of subjects had atherosclerotic symptoms at more than one site. **Smoking** was found to be correlated with lower extremity atherosclerosis, cholesterol and **LDL** cholesterol were correlated with carotid artery lesions and pathological ankle/arm index, and blood pressure was correlated with lower extremity lesions. In contrast with middle-aged populations, individuals with an increasing degree of lesions in the lower extremities had a larger percentage of high glutathione transferase activity than subjects without CVD. Smokers had significantly lower pyridoxal-5-phosphate levels than non-smokers. It is concluded that some heavy smokers might reach an advanced age in good health. **Smoking** was also operative as a risk indicator for lower extremity atherosclerosis in 80-year-old individuals.

175: Atherosclerosis 1990 Jun;82(3):261-5
Alteration of plasma low density lipoprotein from smokers.

Scheffler E, Huber L, Fruhbis J, Schulz I, Ziegler R, Dresel HA

Medizinische Klinik der Universitat Heidelberg, F.R.G.

Thiobarbituric acid reactive substances (**TBARS**) in 38 low density lipoprotein (**LDL**) samples from 21 healthy male non-smokers and 17 smokers (greater than 20 cigarettes per day) were measured before and after oxidation. **TBARS** in the freshly isolated **LDL** from non-smokers and smokers were similar, however, oxidized **LDL** samples from smokers developed nearly twofold more **TBARS** than non-smoker **LDL** samples. 16 **LDL**s from 8 smokers and 8 non-smokers were conditioned in redox-metal containing F-10 medium and subsequently added to P 388 D.1 macrophage cultures. **LDL** dependent cholesteryl ester increase in the P 388 D.1 cells after an 18 h incubation with non-smoker **LDL** was significantly lower than in the cells incubated with smoker **LDL** (P less than 0.01). A higher reacylation rate of cholesterol in P 388 D.1 cells incubated with smoker **LDL** (P less than 0.05) suggests that **LDL**-cholesterol uptake is significantly higher in P 388 D.1 cells incubated with smoker-**LDL** than in P 388 D.1 cultures exposed to non-smoker **LDL**. This finding indicates that **smoking** might contribute to increased shunting of **LDL** into macrophages. The vitamin E content of 6 non-smoker **LDL** samples was significantly higher than that in 6 smoker-**LDL** samples (P less than 0.01). We conclude that the vitamin E/**LDL** ratio may differ significantly in heavy smokers and non-smokers.

PM3000457443

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

176: Am Heart J 1990 Jun;119(6):1267-73

Sustained-release nifedipine (nifedipine-L) suppresses plasma thromboxane B2 and 6-keto prostaglandin F1 alpha in both young male smokers and nonsmokers.

Nakashima Y, Kawashima T, Nandate H, Yashiro A, Kuroiwa A

Second Department of Internal Medicine, University of Occupational and Environmental Health Japan, School of Medicine.

Sustained-release nifedipine (nifedipine-L) (40 mg twice a day) was administered orally to healthy young adult male smokers and nonsmokers for 10 days, and its effects on platelet aggregation, beta-thromboglobulin and platelet factor 4 levels, and plasma **thromboxane B2** (**TxB2**) and 6-ketoprostaglandin F1 alpha (6-Keto-PGF1 alpha) concentrations were studied. The plasma nifedipine-L concentration in smokers (46.0 +/- 7.4 ng/ml) was significantly lower than that in nonsmokers (88.2 +/- 1.2 ng/ml). Nifedipine-L did not affect platelet aggregation induced by adenosine diphosphate, collagen, or epinephrine in either smokers or nonsmokers. The plasma beta-thromboglobulin level on the tenth day of nifedipine-L administration in nonsmokers was lower than that in smokers, but there were no significant differences either with or without nifedipine-L or between nonsmokers and smokers. Nifedipine-L had no effect on the concentration of platelet factor 4 in either smokers or nonsmokers. On the other hand, nifedipine-L significantly decreased the plasma **TxB2** and 6-keto-PGF1 alpha concentrations in both smokers and nonsmokers. Thus we concluded that nifedipine-L suppressed the production of plasma **TxB2** from platelets and also subsequently suppressed the production of 6-keto-PGF1 alpha and that this action was not affected by cigarette **smoking**.

PM3000457444

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

177: Metabolism 1990 Apr;39(4):343-8
Effects of acute smoking and exercise on high-density lipoprotein-cholesterol and subfractions in black female smokers.

Swank AM, Fell RD

Exercise Physiology Laboratory, University of Louisville, KY.

This study investigated the effects of acute bouts of both exercise and **smoking** on high-density lipoprotein-cholesterol subfractions, **HDL**2-C and **HDL**3-C in black females. During two testing trials, seven subjects were exposed to either acute exercise or **smoking**. Treadmill exercise was performed at 70% of heart rate reserve for 15 minutes. Blood samples were taken before, immediately after, and 10 minutes after exercise. The **smoking** trial consisted of subjects **smoking** two cigarettes followed by 30 minutes of non**smoking**. Blood samples were taken before **smoking**, after each cigarette, and after two 15-minute intervals of non**smoking**. The exercise protocol resulted in a 10.8% increase in total **HDL**-C, primarily through an increase in the **HDL**2-C subfraction. The values returned to baseline within 10 minutes after exercise. **Smoking** one cigarette decreased total **HDL**-C by 10%. Neither subfraction was significantly effected by **smoking**; however, the **HDL**3-C subfraction was decreased 11% and **HDL**2-C subfraction was decreased 14.7% from resting values. The maximum reduction in **HDL**3-C subfraction occurred after the **smoking** of the first cigarette, while the maximum reduction in the **HDL**2-C subfraction occurred after the first 15-minute non**smoking** period. Acute cigarette **smoking** was associated with a decrease in total **HDL**-C that was maintained through 15 minutes of non**smoking**. It is suggested that the adverse effect on **HDL**-C by acute **smoking** is a significant contributor to coronary heart disease (CHD) risk in black females. Results further indicate that low-intensity exercise is capable of transiently increasing the total **HDL**-C via an increase in the anti-atherogenic **HDL**2-C subfraction.(ABSTRACT TRUNCATED AT 250 WORDS)

178: J Pharm Pharmacol 1990 Apr;42(4):288-9
Smoking, eicosanoids and ulcerative colitis.

Motley RJ, Rhodes J, Williams G, Tavares IA, Bennett A

Department of Medicine, University Hospital of Wales, Cardiff, UK.

In this study, which is the first of its kind using normal tissue samples that are very difficult to obtain, we have investigated the hypothesis that **smoking** protects against ulcerative colitis by altering the colonic mucosal formation of prostaglandins and related substances. Colonic mucosa biopsied from healthy young men produced prostaglandin E, 6-keto-PGF1 alpha (formed from PGI2), leukotriene B4 and leukotriene C4/D4/E4 as determined by radioimmunoassay. With each substance, the median yield was lower in the group of smokers who smoked 3 cigarettes in the 2 h before biopsy, than in the non-smokers. However, with each eicosanoid the statistical probability approached only the 10% level, but the fact that the trend was the same for all eicosanoids somewhat strengthens the possibility of a real difference between the groups.

PM3000457445

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

179: J R Soc Med 1990 Mar;83(3):146-8
Acute changes in atherogenic and thrombogenic factors with cessation of smoking.

Feher MD, Rampling MW, Brown J, Robinson R, Richmond W, Cholerton S, Bain BJ, Sever PS

Department of Clinical Pharmacology, St Mary's Hospital Medical School, London.

Tobacco **smoking** is associated with alterations in several factors considered to be important in the atherosclerotic process. Thirty chronic smokers were studied 2 weeks before and 2 weeks after complete tobacco withdrawal. Significant reductions in **fibrinogen**, haematocrit, plasma viscosity and whole blood viscosity as well as a significant increase in **HDL**-cholesterol were observed. As these factors are important in both atherogenesis and thrombogenesis, these observations may give insight into tobacco-induced atherosclerotic disease and may be responsible for the more rapid reduction in the incidence of cardiovascular disease that is believed to occur after stopped **smoking**.

180: Eur J Vasc Surg 1990 Feb;4(1):57-61
The influence of smoking and plasma factors on prosthetic graft patency.

Wiseman S, Powell J, Greenhalgh R, McCollum C, Kenchington G, Alexander C, Sian M, Franks P

Department of Surgery, Charing Cross and Westminster Medical School, London, U.K.

The effects of **smoking** and plasma risk factors on the patency of prosthetic femoro-popliteal bypass grafts were investigated in 93 patients entered into a multicentre trial of prosthetic graft materials (70 patients had patent grafts and 23 patients had occluded grafts 2 years after surgery). The **smoking** markers thiocyanate and **fibrinogen** were significantly higher in patients with occluded grafts, whereas **LDL**-cholesterol was significantly higher in patients with patent grafts 2 years after bypass. Based on **smoking** markers, graft patency in smokers was 57% at 2 years by life table, compared to 78% in non-smokers. P less than 0.05. **Fibrinogen** was an important variable, predicting graft occlusion with graft patency in patients with below median **fibrinogen** levels, being 84% at 2 years by life table compared to 51% in those with above median **fibrinogen** levels, P less than 0.025. Although increased levels of **LDL**-cholesterol have been associated with accelerated atherosclerosis, patients with above median levels of **LDL**-cholesterol had improved graft patency (83%) at 2 years compared to patency in patients with below median **LDL**-cholesterol (60%), P less than 0.05. The plasma risk factors associated with the failure of prosthetic grafts are similar to those associated with the failure of saphenous vein grafts, indicating that higher **fibrinogen** levels and **smoking** may contribute to an hypercoagulable state. Greater efforts are needed to stop patients **smoking** after vascular reconstruction.
Publication Types:
Clinical trial

PM3000457446

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

181: Pediatrics 1990 Feb;85(2):155-8
Cigarette smoking-associated changes in blood lipid and lipoprotein levels in the 8- to 19-year-old age group: a meta-analysis.

Craig WY, Palomaki GE, Johnson AM, Haddow JE

Foundation for Blood Research, Scarborough, ME 04074.

In this meta-analysis it was demonstrated that, when compared with nonsmokers of similar age, smokers in the 8- to 19-year-old age group have significantly higher serum levels of triglyceride (+11.8%), very-low-density lipoprotein (V**LDL**)-cholesterol (+12.4%) and **low-density lipoprotein** (**LDL**)-cholesterol (+4.1%) and significantly lower serum levels of **high-density lipoprotein** (**HDL**)-cholesterol (-8.5%) and total cholesterol (-3.7%). All of these **smoking**-associated changes are in the same direction as those found in adults, with the exception of total cholesterol levels, which are significantly increased in adult smokers. The extent to which mean triglyceride, **LDL**-cholesterol, and **HDL**-cholesterol levels are shifted is significantly greater in the 8- to 19-year-old smokers than in adult smokers. The changes in mean total cholesterol levels among smokers in both age groups represent only the net shifts in the lipoprotein fractions and are therefore likely to be a less sensitive indicator of the possible lipid-related excess coronary artery disease risk in smokers.

Publication Types:
Meta-analysis

182: Atherosclerosis 1990 Jan;80(3):209-16
Effects of cigarette smoking and dietary lipids on rat lipoprotein metabolism.

Maida V, Howlett GJ

Russell Grimwade School of Biochemistry, University of Melbourne, Parkville, Vic., Australia.

The effects of cigarette smoke inhalation on rat lipoprotein metabolism have been examined. Rats were subjected to cigarette smoke exposure over a 3-week period (two 1-h sessions/day) using a Bat-Mason inhalation machine. Rats exposed to cigarette smoke showed a decrease in total serum triglyceride and an increase in very low density lipoprotein cholesterol (V**LDL**-C). Administration of cigarette smoke to rats fed a saturated fat and cholesterol enriched diet also led to an increase in V**LDL**-C and a decrease in total serum triglycerides compared to controls. In addition, cigarette smoke exposure to animals fed the lipid enriched diet caused a decrease in high density lipoprotein cholesterol (**HDL**-C). Pair-feeding experiments indicated that the increase in V**LDL**-C and the decrease in **HDL**-C could not be solely attributed to the reduction in food intake and the small decrease in growth rate observed following cigarette smoke exposure. The changes observed in V**LDL**-C and **HDL**-C are at least qualitatively similar to the changes seen in human smokers compared to non-smokers.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

183: Adv Exp Med Biol 1990;273:267-72
Normalization of high density lipoprotein cholesterol following cessation from cigarette smoking.

Moffatt RJ

Department of Nutrition, Food, and Movement Sciences, Florida State University,
Tallahassee 32306.

184: Digestion 1990;46(1):27-34
Cigarette smoking increases gastric luminal prostaglandin F2 alpha and thromboxane B2 in healthy smokers.

Fedi P, Calabro A, Orsini B, Milani S, Zacchi P, Salvadori G, Surrenti C

Department of Clinical Pathophysiology, University of Florence, Italy.

Pentagastrin-stimulated gastric luminal prostaglandin E2 (PGE2), 6-keto-PGF1 alpha, **PGF2** alpha and thromboxane B2 (**TxB2**) were measured using a second antibody solid-phase enzyme immunoassay before, during and after cigarette **smoking** in healthy smokers. **Smoking** significantly increased **PGF2** alpha and **TxB2** concentration and output; in contrast no significant changes were found for PGE2 and 6-keto-PGF1 alpha levels. In addition, cigarette **smoking** caused a significant reduction in gastric juice volume and acid output but did not alter intragastric acidity. These findings may suggest a possible role of prostanoids in the response of the stomach to cigarette **smoking**.

185: Chem Biol Interact 1990;76(1):101-9
Effects of acrolein on human platelet aggregation.

Selley ML, Bartlett MR, McGuiness JA, Ardlie NG

Australian National University, John Curtin School of Medical Research, Division of Clinical Sciences, Woden Valley Hospital, Garran, ACT.

Acrolein, a component of tobacco smoke, potentiated platelet aggregation and increased thromboxane A2 (TXA2) formation caused by thrombin and arachidonic acid (AA). Acrolein produced these effects at concentrations in the range 50-5000 microM. Acrolein had no effect on platelet responses to ADP, epinephrine, collagen or the ionophore A23187. Acrolein increased the mobilization of [3H]arachidonic acid from prelabelled platelets in response to thrombin and arachidonic acid. The increased availability of substrate could partly explain the enhanced production of TXA2 and increased aggregation observed in the presence of acrolein. These findings could provide an explanation for the increased incidence of vascular disease in cigarette smokers.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

186: Nihon Kyobu Shikkan Gakkai Zasshi 1989 Dec;27(12):1495-501
[Effects of nicotine and cigarette smoke extracts on plasma level of complement C3a and C5a, thromboxane B2 and 6-keto PGF1 alpha in rabbits].

[Article in Japanese]

Kihira Y, Kobayashi J, Kitamura S

In the present investigation we measured plasma levels of complement C3a and C5a, thromboxane B2 (**TxB2**) and 6-keto PGF1 alpha in anesthetized rabbits by radioimmunoassay after the intravenous injection of nicotine and cigarette smoke extracts. Plasma levels of complement C3a in rabbits showed a significant increased and reached a maximum value 60 minutes after the intravenous injection of nicotine and cigarette smoke extract. Plasma levels of complement C5a in rabbits showed a significant increase and reached a maximum value 30 minutes after the intravenous injection of nicotine. Plasma levels of complement C5a in rabbits showed a significant increase and reached a maximum value 60 minutes after the intravenous injection of cigarette smoke extract. Plasma levels of **TxB2** in rabbits showed a significant increase after the intravenous injection of nicotine and cigarette smoke extract. Plasma levels of 6-keto PGF1 alpha in rabbits did not show any change after the intravenous injection of nicotine and cigarette smoke extracts. The above results may suggest that the intravenous injection of nicotine and cigarette smoke extracts induces an increase of plasma levels of complement C3a and C5a and **TxB2** in anesthetized rabbits.

187: Atherosclerosis 1989 Nov;80(1):33-9
Effects of age and cigarette smoking on serum concentrations of lipids and apolipoproteins in a male military population.

Cuesta C, Sanchez-Muniz FJ, Garcia-La Cuesta A, Garrido R, Castro A, San-Felix B, Domingo A

Departamento de Nutricion, Facultad de Farmacia, Universidad Complutense, Madrid, Spain.

The effects of age and cigarette **smoking** on lipids and apolipoproteins were studied in men, 20-65 years old, randomly selected from a military population in the Madrid area, Spain. Subjects were classified as non-smokers, medium smokers (10-20 cigarettes/day) and heavy smokers (more than 20 cigarettes/day). **Smoking** prevalence was 58%. Serum apolipoprotein A-I and **HDL**-cholesterol (**HDL**-C) were not age-dependent, while total cholesterol (TC), triglycerides (TG), **LDL**-cholesterol (**LDL**-C) and the TC/**HDL**-C ratio increased with age. None of the variables studied was age-dependent over 30 years. The effects of **smoking** on TC, TG, **LDL**-C, **HDL**-C, TC/**HDL**-C ratio, apolipoprotein A-I, apolipoprotein B, and apo A-I/apo B ratio in the 20-29-year-old group appeared to be prominent in heavy smokers (P values less than 0.001, less than 0.05, less than 0.01, less than 0.05, less than 0.001, less than 0.05, less than 0.01 and less than 0.05, respectively) but not in medium smokers, in which only TG increased significantly (P less than 0.001). Few differences were noted between non-smokers and smokers over 30 although the TC/**HDL**-C ratio did increase in heavy smokers (P less than 0.05).

PM3000457449

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

188: Biochim Biophys Acta 1989 Oct 13;993(1):121-7
Cigarette smoking: profiles of thromboxane- and prostacyclin-derived products in human urine.

Barrow SE, Ward PS, Sleightholm MA, Ritter JM, Dollery CT

Department of Clinical Pharmacology, Royal Postgraduate Medical School, Hammersmith Hospital, London, U.K.

Thromboxane (TX) B2, 2,3-dinor-**TXB2**, 11-dehydro-**TXB2**, 6-oxoprostaglandin (PG)F1 alpha and 2,3-dinor-6-oxo-PGF1 alpha were measured in 24 h urine samples obtained from 30 apparently healthy chronic cigarette smokers and 37 closely matched non-**smoking** control subjects. Samples were analysed using a newly developed assay based on immunoaffinity chromatography and capillary column gas chromatography/electron capture negative ion chemical ionisation mass spectrometry. There were significant and comparable increases in the excretion rates of both 2,3-dinor-**TXB2** and 11-dehydro-**TXB2** in the **smoking** compared with the non-**smoking** group (2P less than 0.001). Excretion rates of 2,3-dinor-**TXB2** were 418 +/- 35 and 265 +/- 26 pg/mg creatinine in the two groups, respectively. 11-Dehydro-**TXB2** excretion rates were 440 +/- 54 and 221 +/- 18 pg/mg creatinine, respectively (mean +/- S.E.). There were significant (2P less than 0.05) positive correlations between average reported cigarette consumption and excretion of both thromboxane metabolites. There were small but significant (2P less than 0.02) increases in the excretion rates of both 6-oxo-PGF1 alpha and 2,3-dinor-6-oxo-PGF1 alpha in the **smoking** compared with the non-**smoking** group. There was no significant difference in the rates of excretion of **TXB2** in the two groups. The effects of acute cigarette smoke exposure (five cigarettes in 2 h) was also studied in four normally non-**smoking** healthy volunteers. There was no significant change in the excretion rate of any of the eicosanoids measured during control and **smoking** periods (at least 2 weeks apart), indicating that increased TXA2 biosynthesis in chronic smokers is unlikely to be a consequence of acute platelet activation.

189: An Esp Pediatr 1989 Oct;31(4):331-5
[The Fuenlabrada study: smoking habits in children and adolescents. Effect on various cardiovascular risk factors].
[Article in Spanish]

Munoz Calvo MT, Plaza Perez I, Madero Medrano R, Lopez Martinez D, Otero de Becerra J, Hidalgo Vicario I, Baeza Minguez J, Cenal Gonzalez-Fierro MJ, Parra Martinez I, Cobaleda Rodrigo A, et al

Hospital Nino Jesus, Universidad Autonoma, Madrid.

We studied 1,274 healthy children of both sexes from 10 until 18 years of age, in Fuenlabrada, Madrid. We knew the tobacco consumption by means of direct asking to the children, without the presence of their parents. We studied the **smoking** habit of their parents by means of inquiries. The percentage of smoker children was 30% (24% of them had smoker parents, and 6% did not). We studied the tobacco influence in several parameters of cardiovascular risk; it was found that C-**HDL** levels in the smoker children were 5 mg/dl lower than the non-smokers, and the ratio C-**LDL**/C-**HDL** in the smokers was 1,2 times greater than in the non-smokers.
Review
Review literature

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

190: Chung Hua Chieh Ho Ho Hu Hsi Tsa Chih 1989 Oct;12(5):275-7, 318
[Effects of smoking on human health].
[Article in Chinese]

Du BY

In this study, 30 cases of male smokers aged 35.7 +/- 5.2 years mean and 30 male nonsmokers aged 36.6 +/- 6.8 years were selected from a factory. Before the assay, everyone smoked one pack of cigarette in a day, after that these tests were done. The experimental results as follows. 1. Comparing with control group, the levels of IgG and IgM in serum of **smoking** group are lower. It was shown that **smoking** has an inhibitive effect on phagocytosis and bactericidal of AM, so **smoking** has a damaging and prohibitive effect on the immunity of the body. 2. **Smoking** increases the level of serum IgE. 3. The increase of the level of CIC in serum in **smoking** individuals suggested that the defensive function decreases and the infectious susceptibility increases. So we should pay greatest attention to the occurrence of allergic disease of type III. 4. **Smoking** increases the level of serum elastase. 5. The level of **TXB2** in human plasma of smokers increases. The result suggested that smoke plays an important role in cardiovascular diseases. 6. The decrease of the level of cAMP in the plasma of smokers may be related to the release of some mediators. 7. The increase of the level of vWF in the plasma of smokers may suggest that there are lesions in the endothelium of pulmonary blood vessels.

191: Pathol Biol (Paris) 1989 Oct;37(8):937-9
[Nicotine gum and lipid profile].
[Article in French]

Lagrue G, Grimaldi B, Martin C, Demaria C, Jacotot B

Centre d'Aide au Sevrage Tabagique INSERM U.139, Hopital Henri-Mondor, Creteil,France.

Smoking promotes for atherosclerosis by several mechanisms and particularly its actions on lipid metabolism; nicotine liability is well established. In one patient the use of nicotine-gum was reported to increase total cholesterol and **LDL** cholesterol. We studied lipid modifications in 14 voluntary students, heavy smokers (greater than 20 cigarettes/day) and nicotine dependent (Fagerstrom test; score greater than 7). They gave up **smoking** and received in double blind study either 2 mg nicotine-gum, or placebo-gum (8-12 gums a day for one month). Total and **HDL** cholesterol (chol.), triglycerides (TG) were measured at day 0, day 30 and day 60. Giving up **smoking** was ascertained by CO-analyser. At day 30 total chol and TG were unmodified, and **HDL** chol appeared slightly increased. At day 60 **HDL** and **LDL** chol were significantly improved. So in nicotine-dependent smokers, by giving up **smoking** and receiving 2 mg nicotine-gum, lipid patterns are not worsened but improved.
Clinical trial
Controlled clinical trial

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

192: Nihon Kyobu Shikkan Gakkai Zasshi 1989 Oct;27(10):1193-7
[The influence of cigarette smoke on metabolism of eicosanoids in rat lung in terms of variation of 15-hydroxyeicosatetraenoic acid and 11-dehydrothromboxane B2].

[Article in Japanese]

Nagase T, Fukuchi Y, Shimizu T, Yamaoka M, Matsuse T, Hirose T, Suruda T, Jo C, Ishida K, Orimo H

We investigated the effects of cigarette **smoking** on metabolism of two eicosanoids, 15-hydroxyeicosatetraenoic acid (15-HETE) and 11-dehydrothromboxane B2 (11-dehydro-**TXB2**) in the lung. Twelve female Wistar rats aged between 5 and 6 weeks were chosen and the **smoking** group (SG, n = 6) was compared to the control group (CG, n = 6). Cigarette smoke exposure was performed using a Hamburg-II inhalation apparatus and the dose was 10 cigarettes in 30 min. Bronchoalveolar lavage (BAL) was conducted 30 min after **smoking** exposure and the recovered BAL fluid was centrifuged at 3000 rpm for 10 min. The levels of 15-HETE and 11-dehydro-**TXB2** of the supernatant were measured by radioimmunoassay in each sample. Recovered 15-HETE significantly increased in SG (SG: 490 +/- 109 pg, CG: 191 +/- 63 pg, p less than 0.05), while there was no significant difference in recovered protein (SG: 2.64 +/- 0.50 mg, CG: 2.23 +/- 0.10 mg), 11-dehydro-**TXB2** (SG: 128 +/- 13 pg, CG: 156 +/- 7 pg). We conclude that acute cigarette smoke exposure increases recovered BAL fluid 15-HETE, a potent inflammatory mediator and that 15-HETE in BAL fluid may indicate lung injury induced by **smoking**.

193: Atherosclerosis 1989 Oct;79(2-3):245-52
Cigarette smoking renders LDL susceptible to peroxidative modification and enhanced metabolism by macrophages.

Harats D, Ben-Naim M, Dabach Y, Hollander G, Stein O, Stein Y

Department of Medicine, Hadassah University Hospital, Jerusalem, Israel.
The effect of cigarette **smoking** on peroxidation of plasma low density lipoprotein (**LDL**) was studied in 16 smokers aged 23-56 years; 12 nonsmokers of similar age served as controls. The smokers were asked to refrain from **smoking** 24-40 h prior to testing. Peroxidation was assessed by determination of thiobarbituric acid reactive substances (**TBARS**) in fresh plasma and **LDL** and by an increase in 125I-**LDL** metabolism by peritoneal macrophages. There was no difference in **TBARS** in freshly prepared plasma or **LDL** of smokers and nonsmokers. However, **LDL** of smokers, conditioned by incubation with bovine aortic smooth muscle cells (SMC), had 2-fold or higher **TBARS** values when compared to SMC conditioned **LDL** of nonsmokers. 2-4-fold higher **TBARS** values were seen also in SMC conditioned **LDL** when the comparison was made between **LDL** isolated from plasma before **smoking** of 6-7 cigarettes (time 0), and **LDL** of the same individual isolated from plasma 90 min thereafter. The metabolism of SMC conditioned 125I-**LDL** by peritoneal macrophages was examined; **LDL** isolated from plasma of smokers at time 0 was metabolized twice as avidly as **LDL** of nonsmokers and a further increase was seen with **LDL** isolated 90 min after acute **smoking**. The present results indicate that cigarette **smoking** renders plasma **LDL** more susceptible to subsequent peroxidative modification by cellular elements.

PM3000457452

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

194: Clin Genet 1989 Oct;36(4):266-8
Smoking and reverse cholesterol transport: evidence for gene-environment interaction.

Kaprio J, Ferrell RE, Kottke BA, Sing CF

Department of Human Genetics, University of Michigan Medical School, Ann Arbor.

195: Nippon Eiseigaku Zasshi 1989 Aug;44(3):725-32
[An epidemiological study on the relationships among HDL-cholesterol, smoking and obesity].
[Article in Japanese]

Misawa K, Matsuki H, Kasuga H, Yokoyama H, Hinohara S

The relationships among high-density lipoprotein cholesterol (**HDL**-C) and other serum lipid items, and active **smoking**, passive **smoking**, obesity, alcohol drinking and working status were investigated. This study was performed both in healthy adults and in schoolchildren. The adult group was sampled at random from those who were diagnosed to be healthy by medical examination at the Automated Multiphasic Health Testing and Services Center in Tokai University Hospital, and the schoolchildren group was selected with regular health examinations in a primary school in Tokyo. In the case of adults, it was found that the greater the value of triglyceride (TG), the greater the number of cigarettes smoked. On the other hand, **HDL**-C decreased with increasing cigarette **smoking**. Obesity level increased with increasing values of TG, total cholesterol (TC) and low density lipoprotein (**LDL**-C) but in the case of **HDL**-C, the value decreased. Alcohol drinking made the **HDL**-C level increase. Although the **HDL**-C level increased slightly with obesity, the relationship between **HDL**-C and passive **smoking** was not clear in the case of schoolchildren.

PM3000457453

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

196: Clin Exp Pharmacol Physiol 1989 Jul;16(7):597-605

Whole blood aggregation and plasma lyso-PAF related to smoking and atherosclerosis.

Sturm MJ, Strophair JM, Kendrew PJ, Vandongen R, Beilin LJ, Taylor RR

Department of Medicine, University of Western Australia.

1. Aggregation of diluted whole blood (impedance method) and thromboxane B2 production during aggregation were measured in cigarette smokers and non-smokers, aged 41-68 years, with (n = 14) and without (n = 15) major symptomatic peripheral vascular disease. The plasma level of the lyso derivative of platelet activating factor (lyso-PAF) was also measured using a bioassay with 14C-serotonin labelled rabbit platelets, after extraction and acetylation to active PAF. 2. Aggregation to ADP and collagen was significantly less in non-smokers without vascular disease (n = 8) than in the other three groups (P less than 0.01; ANOVA). Thromboxane B2 production was not significantly different between the groups. There was no significant difference in plasma lyso-PAF between groups. No change was found in any variable after smokers smoked two cigarettes. 3. In these older age subjects, both vascular disease and the **smoking** habit were associated with greater whole blood aggregation. However, current **smoking** and the **smoking** of two cigarettes did not affect aggregation in subjects with vascular disease and plasma lyso-PAF levels were not consistently related to either **smoking** or vascular disease.

PM3000457454

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

197: BMJ 1989 Mar 25;298(6676):784-8
Cigarette smoking and serum lipid and lipoprotein concentrations: an analysis of published data.

Craig WY, Palomaki GE, Haddow JE

Foundation for Blood Research, Scarborough, ME 04074.

To examine the association between cigarette **smoking** in adults and serum lipid and lipoprotein concentrations the results of 54 published studies were analysed. Overall, smokers had significantly higher serum concentrations of cholesterol (3.0%), triglycerides (9.1%), very low density lipoprotein cholesterol (10.4%), and low density lipoprotein cholesterol (1.7%) and lower serum concentrations of high density lipoprotein cholesterol (-5.7%) and apolipoprotein AI (-4.2%) compared with nonsmokers. Among non-smokers and light, moderate, and heavy smokers a significant dose response effect was present for cholesterol (0, 1.8, 4.3, and 4.5% respectively), triglycerides (0, 10.7, 11.5, and 18.0%), very low density lipoprotein cholesterol (0, 7.2, 44.4, and 39.0%), low density lipoprotein cholesterol (0, -1.1, 1.4, and 11.0%), high density lipoprotein cholesterol (0, -4.6, -6.3, and -8.9%), and apolipoprotein AI (0, -3.7 and -5.7% in non-smokers and light and heavy smokers). These dose response effects may provide new evidence for a causal relation between exposure to cigarette smoke and changes in serum lipid and lipoprotein concentrations whether as a direct result of physiological changes or of dietary changes induced by **smoking**. Adequate prospective data to estimate the excess risk of coronary artery disease existed only for cholesterol concentration. When that information was combined with data from the present study, and given that smokers as a group face an average overall excess risk of coronary artery disease of 70%, it was estimated that the observed increased serum cholesterol concentration in smokers may account for at least 9% of that excess risk. Furthermore, the dose response effect of **smoking** on serum cholesterol concentration suggests a gradient of increased absolute risk of coronary artery disease between light and heavy smokers.

Comments:
Comment in: BMJ 1989 May 13;298(6683):1312

198: Indian Heart J 1989 Mar-Apr;41(2):92-4
Effect of cigarette smoking on serum total cholesterol and high density lipoprotein cholesterol in normal subjects and coronary heart patients.

Tiwari AK, Gode JD, Dubey GP

In the present study, 51 apparently normal volunteers and 34 clinically established coronary heart disease cases were studied. 21 out of 51 normal, and 16 out 34 coronary heart disease cases were cigarette smokers. The cases were divided in two age groups--20 to 40 years, the younger age group and 41 to 60 years, the older age group. Total serum cholesterol and high-density lipoprotein cholesterol of all the cases were determined. The ratio of total cholesterol to high-density lipoprotein cholesterol was significantly higher in all the **smoking** normal and coronary heart disease smokers. Hence, the higher levels of total cholesterol to high density lipoprotein cholesterol ratio appears to be one of the important parameters to ascertain the development of coronary heart disease in cigarette smokers.

PM3000457455

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

199: Eur Heart J 1989 Mar;10(3):196-202
Published erratum appears in Eur Heart J 1991 Oct;12(10):1151
On the within-population relationship between nutrition and serum lipids: the B.I.R.N.H. study.

Kesteloot H, Geboers J, Joossens JV

Department of Epidemiology, School of Public Health, Leuven, Belgium.

A randomized study was performed in Belgium concerning the relationship between diet and serum lipids in 5485 men and 4856 women with a mean age of 49 years. In men 17.3% of total energy was provided by saturated fat, 15.2% by monounsaturated fat and 7.5% by polyunsaturated fat. The fat intake in women was very similar. The P/S ratio was 0.51 in men and 0.52 in women. The alcohol intake was significantly higher in men (5.2% of total energy) than in women (2% of total energy). In men and women total serum cholesterol increased with saturated fat intake (p less than 0.001) and decreased with polyunsaturated fat intake (p less than 0.01). Saturated fat intake raised the **HDL**-cholesterol level in men and women (p less than 0.001) and monounsaturated fat raised it in men only (p less than 0.01). Dietary cholesterol increased the **HDL**-cholesterol level in women only (p less than 0.01). **HDL**-cholesterol increased with alcohol consumption (p less than 0.001) and decreased with cigarette **smoking** (p less than 0.001). All these changes were adjusted for differences in age, height and weight. The study confirms the existence, within a population, of a significant relationship between fat intake and serum lipid levels.

200: J Tongji Med Univ 1989;9(4):222-7
Effects of cigarette smoking on hemodynamics and hypoxic pulmonary vasoconstriction: role of prostaglandins and leukotrienes.

Chen G, Wang DX

This study investigated the role of prostaglandins (PGs) and leukotrieres (LTs) in hypoxic pulmonary vasoconstriction (HPV) and in cigarette **smoking**-induced changes in hemodynamics and HPV in Wistar rats. Selective LTD4-LTE4 receptor antagonist LY-171883 (LY) inhibited HPV by 71.8%, while cyclooxygenase inhibitor indomethacin (IND) augmented HPV. The results indicate that LTs mediate HPV in Wistar rats. **Smoking** increased the level of **TXB2** over control by 143.6% in plasma and 69.2% in lung tissue, concomitantly, pulmonary and systemic vascular resistance (PVR and SVR) were increased by 38.7% and 46.7%, respectively. Both LY and IND prevented the **smoking**-induced increase of PVR and SVR. After **smoking** HPV increased twofold. The increase of HPV was abolished by LY, but not by IND. Our results suggest that **smoking** leads to pulmonary and systemic vasoconstriction partly mediated by TXA2 and LTs; **smoking** also leads to an augmentation of HPV, and LTs play an important role in it.

PM3000457456

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

201: Pathology 1989 Jan;21(1):46-50
Levels of serum cholesterol, triglyceride, HDL-cholesterol, apoproteins A-I and B, and plasma glucose, and prevalence of diastolic hypertension and cigarette smoking in Papua New Guinea highlanders.

Scrimgeour EM, McCall MG, Smith DE, Masarei JR

Faculty of Medicine, University of Papua New Guinea.

Coronary heart disease (CHD) is rare in Papua New Guinea (PNG) highlanders. Fifty-two men and 69 women randomly selected from three rural communities and a low socioeconomic urban community in the Eastern Highlands Province were assessed for hyperlipidemia, diabetes mellitus, diastolic hypertension and cigarette **smoking**. There was no significant difference between the findings in the rural and urban groups. The mean fasting levels of serum cholesterol, **HDL** cholesterol and apoproteins A-I and B were significantly lower (p less than 0.001) than those of rural Australians in a comparative study but the serum triglyceride levels were significantly higher in men less than 30 yr and women less than 40 yr of age. There was no significant difference in the serum cholesterol levels in men and women, and the levels of serum cholesterol and triglyceride did not rise with age. The mean fasting levels of plasma glucose were generally lower in PNG subjects and only two (1.7%) had diabetes mellitus. The proportions of highlanders who had diastolic hypertension or who smoked cigarettes were similar to those of Australian populations generally. The low incidence of CHD in PNG highlanders is probably related to the low serum cholesterol and apoprotein B levels, in turn probably related to their basically vegetarian diet and physically active life-style.

202: Atherosclerosis 1988 Nov;74(1-2):85-9
Effects of cessation of smoking on serum lipids and high density lipoprotein-cholesterol.

Moffatt RJ

Department of Movement Science and Physical Education, Florida State University,Tallahassee 32306-3045.

This study examined the effect of cessation of **smoking** on serum lipid and lipoprotein levels. Twenty-six females who smoked a minimum of 20 cigarettes per day for the past 5 years served as volunteers. Twelve subjects abstained from **smoking** for a period of 60 days (ex-smokers). Six stopped **smoking** for 30 days then resumed **smoking** for an additional 30 days (re-smokers). Eight subjects continued to smoke for the entire 60 days (smokers). Additionally, 10 females who had never smoked served as non-**smoking** controls (non-smokers). Pre-cessation **HDL**-C levels for all smoker groups were 15-20% (P less than 0.05) below those of non-smokers. By day 30 of cessation **HDL**-C levels of ex-smokers and re-smokers significantly increased by 5.7 and 10.5 mg/dl, respectively, and were significantly higher than those of smokers. At day 60, **HDL**-C of ex-smokers increased another 6.8 mg/dl to 63.9 mg/dl while levels of re-smokers returned to pre-cessation levels (50.7 mg/dl). The findings of this study suggest that low levels of **HDL**-C associated with **smoking** in females do not appear to be cumulative and can be reversed in as little as 30 days.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

203: BMJ 1988 Oct 15;297(6654):955-7
Published erratum appears in BMJ 1988 Dec 3;297(6661):1449

Vasoactive and atherogenic effects of cigarette smoking: a study of monozygotic twins discordant for smoking.

Lassila R, Seyberth HW, Haapanen A, Schweer H, Koskenvuo M, Laustiola KE

Wihuri Research Institute, Helsinki, Finland.

The mechanism by which atherosclerotic disease is induced by cigarette **smoking** has not yet been identified unequivocally. Chronic cigarette **smoking** and the generation of vasoactive prostanoids and the size of carotid atherosclerotic plaques were studied in nine pairs of identical male twins discordant for **smoking** for over 20 years. The urinary excretion of 2,3-dinor-thromboxane B2 (thromboxane B2 metabolite) of the **smoking** twin was significantly higher (on average 1.8 times higher) in every pair and that of 2,3-dinor-6-keto-prostaglandin F1 alpha (prostacyclin metabolite) was significantly higher (on average 1.3 times higher) in eight of the nine pairs. The ratio of excretion of these metabolites was significantly higher, being 4.0 (95% confidence interval 2.7 to 5.4) among the smokers compared with 2.9 (2.1 to 3.8) among the non-smokers, thus favouring a mechanism of vasoconstriction. Excretion of the thromboxane B2 metabolite was related to the urinary concentrations of nicotine metabolites. Atherosclerotic plaques detected by ultrasonography in the carotid arteries were significantly larger among smokers but did not correlate with the urinary excretion of prostacyclin and thromboxane B2 metabolites or intensity of **smoking**. **Smoking** was concluded to induce activation of platelets by an effect mediated by nicotine. The increased prostacyclin production, on the other hand, suggested a compensatory mechanism for the general vasoconstrictive properties of cigarette **smoking**.

PM3000457458

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

204: Am J Obstet Gynecol 1988 Oct;159(4):820-5

Effects of smoking on serum lipoproteins and bone mineral content during postmenopausal hormone replacement therapy.

Jensen J, Christiansen C

Department of Clinical Chemistry, University of Copenhagen, Glostrup Hospital, Denmark.

We examined the effect of **smoking** on the treatment response in serum estrogens, serum lipids and lipoproteins, and bone mineral content in 110 postmenopausal women treated for 2 years with either percutaneous or orally administered combined hormones or placebo and followed up by examinations every 3 months. Serum estradiol and estrone levels during oral hormone administration were lower in smokers than in nonsmokers, whereas no differences related to **smoking** habits were observed during percutaneous hormone administration. Serum total and low-density lipoprotein cholesterol were significantly reduced in both smokers and nonsmokers receiving hormones, but the response in smokers was only half that observed in nonsmokers (not significant). When the impact of the route of hormone administration was examined in relation to **smoking** habits, the response in serum total and low-density lipoprotein cholesterol in smokers receiving oral hormones was significantly lower (p less than 0.05) than that observed in nonsmokers. No differences in serum lipids or lipoproteins were observed between smokers and nonsmokers receiving percutaneous hormones. The response in bone mineral content in smokers and nonsmokers receiving percutaneous hormones and placebo was not significantly different, although the overall response differed significantly in the two groups (p less than 0.001). In contrast, the response in smokers receiving oral hormones was significantly lower than that observed in the corresponding nonsmokers (p less than 0.01). We conclude that **smoking** greatly affects the response on circulating levels of estrogens in postmenopausal women treated with orally administered hormone replacement therapy and that the subsequent treatment response on serum lipids and lipoproteins and on bone mineral content is reduced accordingly. The study suggests that alternative routes of administration should be considered when postmenopausal estrogen therapy is instituted in women who smoke.

Publication Types:
Clinical trial
Controlled clinical trial

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

205: Clin Cardiol 1988 Aug;11(8):538-40

Effects of acute smoking on the hemostatic system in humans.

Vicari AM, Margonato A, Macagni A, Luoni R, Seveso MP, Vicedomini G, Pozza G

Department of Medicine, Istituto Scientifico San Raffaele, Milan, Italy.

Habitual **smoking** is one of the best established risk factors for cardiovascular disease. The pathogenesis of smoke-induced damage is not so well clarified, but it probably includes--among some other aspects--an activation of the hemostatic system. Recently it has been shown that **smoking** a single cigarette can significantly decrease the coronary blood flow in coronary patients as well as in normal subjects. We tested the hypothesis that the acute effects of smoke are mediated by the hemostatic system. Seven healthy male volunteers, aged 20-40 years (mean 32 +/- 6 years), entered the study. All were habitual smokers, but had abstained from **smoking** in the 12 hours preceding the test. After lying in absolute rest for about 30 minutes, each subject smoked a cigarette containing 1.2 mg of nicotine. Immediately before and after **smoking**, blood was drawn by clear venipuncture for the evaluation of the following hemostatic variables: collagen-induced platelet aggregation by the method of Born; thromboxane B2 (**TxB2**) production by platelets stimulated with collagen, radioimmunoassay (RIA); plasma beta thromboglobulin (TG) (RIA); plasma fibrinopeptide A (FPA) (RIA); plasma fibrinolytic activity in the euglobulin fraction (NEF) (fibrin plate method). The following results, respectively before and after **smoking**, were observed: collagen-induced platelet aggregation 55 +/- 3 vs. 57 +/- 6%; **TxB2** 100.5 +/- 5.9 vs. 90.3 +/- 9.0 ng/10(8) platelets; plasma beta-TG 20.8 +/- 2.2 vs. 19.2 +/- 2.3 ng/ml; plasma FPA 2.3 +/- 0.3 vs. 2.2 +/- 0.1 ng/ml; NEF, lysis diameter 16.8 +/- 1.6 vs. 16.7 +/- 1.7 mm; NEF + C1 inhibitor lysis diameter 8.8 +/- 0.7 vs. 9.1 +/- 0.7 mm.(ABSTRACT TRUNCATED AT 250 WORDS)

PM3000457460

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

206: Am J Obstet Gynecol 1988 Jun;158(6 Pt 2):1606-11
Effects of estrogen dose and smoking on lipid and lipoprotein levels in postmenopausal women.

Krauss RM, Perlman JA, Ray R, Petitti D
Lawrence Berkeley Laboratory, University of California, Berkeley 94720.

The joint effects of conjugated estrogen use, age, body mass index, and **smoking** on plasma lipid and lipoprotein levels were assessed in 585 women who used oral estrogen and 1093 women who did not who participated in the Walnut Creek Contraceptive Drug Study. Whether administered daily or cyclically, conjugated estrogen was associated with reductions in low-density lipoprotein cholesterol levels and increases in **high-density lipoprotein** cholesterol and triglyceride levels. The adjusted mean low-density lipoprotein cholesterol concentration was 132 mg/dl for women who used conjugated estrogen in a dose greater than or equal to 1.25 mg/day; the adjusted corresponding mean concentration was 147 mg/dl for postmenopausal women who did not use estrogen. A dose-response pattern was demonstrated between conjugated estrogen and **low-** and **high-density lipoprotein** cholesterol levels. A maximum low-density lipoprotein cholesterol level reduction was reached at a dose of 1.25 mg, suggesting a saturation phenomenon. Stepwise dose-response increases in high-density lipoprotein cholesterol levels were also found with estrogen therapy, with a maximum increase of 8 to 10 mg/dl observed with the 1.25 mg dose. Estrogen-related rises in **low-density lipoprotein** cholesterol levels and decreases in high-density lipoprotein cholesterol levels were offset by 2 to 3 mg/dl in women who smoked. It may be concluded, therefore, that among postmenopausal women, low-risk lipoprotein profiles as assessed by low- and high-density lipoprotein cholesterol levels are found in nonsmokers whose postmenopausal hormone therapy includes the equivalent of a conjugated estrogen dose of 1.25 mg.

207: JAMA 1988 May 20;259(19):2857-62
Low-level cigarette smoking and longitudinal change in serum cholesterol among adolescents. The Berlin-Bremen Study.

Dwyer JH, Rieger-Ndakorerwa GE, Semmer NK, Fuchs R, Lippert P

Department of Preventive Medicine, University of Southern California School of Medicine, Pasadena.

The current study was conducted to determine if smokers and nonsmokers differ in serum concentrations of high-density lipoprotein cholesterol (**HDL**-C) before **smoking** initiation and if a decline in **HDL**-C levels could be detected among adolescents during the first two years of **smoking**. Changes in **HDL**-C levels and **smoking** were observed longitudinally in 1983, 1984, and 1985 among 691 seventh and eighth graders (age range, 12 to 14 years) from two German cities; 82% were nonsmokers at baseline. For these baseline nonsmokers, no differences in baseline **HDL**-C concentrations were found between those who became smokers and those who remained nonsmokers. In contrast, those who became light (one to 39 cigarettes per week) or moderate (greater than or equal to 40 cigarettes per week) smokers by one or two years after the initial examination evidenced lower mean **HDL**-C concentrations relative to persistent nonsmokers at follow-up, constituting a decrement of -0.016 mmol/L [SE = .035] (-0.6 mg/dL) [SE = 1.4] for light smokers and -0.114 mmol/L [SE = .064] (-4.4 mg/dL) [SE = 2.5] for moderate smokers. These findings suggest that short-term exposure to cigarette smoke at low levels may have atherogenic consequences.

PM3000457461

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

208: Can J Cardiol 1988 Mar;4(2):102-7
Smoking, alcohol consumption, lipid and lipoprotein levels.

Lupien PJ, Moorjani S, Jobin J, Dagenais GR,Fleury LA,Robitaille NM, Rochon J

Centre de recherche sur les maladies lipidiques, Centre hospitalier de l'Universite Laval, Ste-Foy, Quebec.

The lipid profiles of 1165 French Canadian men (aged 42 to 59 years) were studied and related to drinking and **smoking** habits. Alcohol consumption and **smoking** were closely related, smokers consuming twice as much alcohol as non-smokers. When relative body weight, total cholesterol, triglyceride and alcohol consumption were controlled in a covariate analysis, plasma levels of high density lipoprotein (**HDL**) cholesterol, **HDL**2 and **HDL**3 differed significantly between smokers, ex-smokers and nonsmokers. Ex-smokers had higher levels of **HDL** cholesterol than nonsmokers who had higher levels than smokers. The higher levels of **HDL** in ex-smokers could be explained by the confounding effects of alcohol intake. Alcohol users had significantly higher levels of **HDL** cholesterol, **HDL**2 and **HDL**3 than nondrinkers. Men who drank the equivalent of more than 3 ounces of absolute alcohol per week had significantly higher levels of **HDL** cholesterol and **HDL**3 than those who drank less than 3 ounces or did not drink at all. **HDL**2 levels were only significantly different between nondrinkers and those who consumed more than 3 ounces per week. These results show that **smoking** and alcohol have strong but opposing effects on **HDL** and its subfractions in middle-aged French Canadian men.

209: Chung Hua Hsin Hsueh Kuan Ping Tsa Chih 1988 Feb;16(1):16
[Serum thiocyanate and HDL levels and their subgroup levels].

[Article in Chinese]

Hu ZX

210: Vasa 1988;17(2):84-8
Effect of high and low-dose aspirin on circulating endothelial cells.

Sinzinger H, Rauscha F, Fitscha P, Kaliman J

211: Am J Public Health 1988 Jan;78(1):100
Smoking and risk of gallstone disease.

Math MV

Publication Types:
Letter

PM3000457462

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

212: Am Heart J 1988 Jan;115(1 Pt 2):267-71
Cigarette smoking and hemostatic function.

FitzGerald GA, Oates JA, Nowak J

Division of Clinical Pharmacology, Vanderbilt University, Nashville, TN.

Epidemiologic studies clearly link cigarette **smoking** with vasoocclusive cardiovascular disease. Postmortem studies provide evidence of accelerated atherogenesis in asymptomatic smokers. However, the rapid regression of cardiovascular risk within the first year of quitting **smoking** is difficult to explain solely in terms of vascular disease. Recent evidence indicates that plasma **fibrinogen**, which has been prospectively associated with the risk of ischemic heart disease, is elevated in smokers. Similarly, results from studies investigating thromboxane metabolite excretion in urine confirm those involving radiolabeled platelet turnover, suggesting that platelets are activated in the circulation of chronic smokers. Altered hemostatic function, either as a direct result of **smoking** or caused by **smoking**-induced vascular damage, may account for the more rapidly reversible component of cardiovascular risk observed in chronic smokers.

Publication Types:
Review
Review, tutorial

213: Nahrung 1988;32(10):961-4
Penetration of malonic dialdehyde on filtration of tobacco smoke.

Witas T, Sledziewski P

Chemical Department of Sea Fisheries Institute of Maritime Academy in Szczecin, Poland.

It has been found that **malonic dialdehyde** penetrates through the filters of cigarettes. The filter cigarettes, such as "Club", "F6", "Cabinet", "Semper" and "Kenton" as well as non-filter cigarettes, namely "Salem", "Real" and "Karo" generate malonic dialdehyde during **smoking**, in amounts ranging from 15.6 to 44.3 mg/kg, i.e. from 20.4 to 44.3 mg/kg for cigarettes with filters and from 15.6 to 27.1 mg/kg for non-filter cigarettes.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

214: Exp Lung Res 1988;14(6):727-42

Acute cigarette smoke exposure alters lung eicosanoid and inflammatory cell concentrations in rabbits.

Witten ML, Quan SF, Sobonya RE, Bruck D, Devine L, Lemen RJ

Department of Physiology, University of Arizona College of Medicine, Tucson.

We studied lung clearance of technetium-labeled diethylenetriamine pentaacetic acid [(99mTc]DTPA), plasma and bronchoalveolar lavage fluid (BALF) concentrations of 6-keto-PGF1 alpha (stable metabolite of prostacyclin, prostaglandin I2, PGI2), **TxB2** (stable metabolite of thromboxane A2, TxA2), and leukotriene B4 (LTB4), and inflammatory cells as indices of lung injury in rabbits exposed to cigarette smoke (CSE). Thirty-one rabbits were randomly assigned to four groups: control sham exposure (SS, n = 6), sham smoke ibuprofen-pretreated (SS-I, n = 7), CSE (n = 6), and CSE ibuprofen-pretreated (CSE-I, n = 12). Ibuprofen, a cyclooxygenase eicosanoid inhibitor, was administered as a single daily intramuscular injection (25 mg/kg) for 7 d before the experiment. Cigarette or sham smoke was delivered by syringe in a series of 5, 10, 20, and 30 tidal volume breaths with a 15-min counting period between each subset of breaths to determine [99mTc]DTPA biological half-life (T1/2). The CSE-I group was retrospectively divided into rabbits who survived the 30-breath subset (CSE-IL, n = 6) and those who died during the 30-breath CSE (CSE-ID, n = 6). In the CSE, CSE-IL, and CSE-ID groups, [99mTc]DTPA T1/2 as well as BALF LTB4 levels were significantly decreased. Plasma and BALF 6-keto-PGF1 alpha increased in CSE rabbits compared to the other groups. Alveolar macrophages were lower in the CSE-ID rabbits than in the CSE-IL group. CSE and CSE-IL BALF lymphocyte levels were decreased compared to SS values. Our data indicate that acute CSE is associated with significant increases in 6-keto-PGF1 alpha and decreases in LTB4 as well as a significant reduction in lymphocytes. Furthermore, pretreatment with ibuprofen before CSE was associated with severe lung injury in half of the rabbits. The severity of lung injury may be related to a combination of a lower number of alveolar macrophages and blockade of lung PGI2.

PM3000457464

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

215: Am J Epidemiol 1987 Oct;126(4):629-37
Lipoproteins as mediators for the effects of alcohol consumption and cigarette smoking on cardiovascular mortality: results form the Lipid Research Clinics Follow-up Study.

Criqui MH, Cowan LD, Tyroler HA, Bangdiwala S, Heiss G, Wallace RB, Cohn R

Because alcohol consumption is associated with increased high density lipoprotein (**HDL**) cholesterol and decreased low density lipoprotein (**LDL**) cholesterol, and cigarette **smoking** is associated with lower **HDL** cholesterol and higher **LDL** cholesterol, there has been speculation that the protective effect of moderate alcohol consumption and/or the noxious effect of cigarette **smoking** for cardiovascular disease might be mediated in large part by a lipoprotein mechanism. The authors examined this question in a prospective study of 7,461 men and women in 10 North American populations initially seen in 1972-1976 and followed for an average of 8.5 years. Moderate alcohol consumption was weakly protective for cardiovascular disease, while cigarette **smoking** was strongly and significantly associated with cardiovascular disease mortality. As expected, **LDL** cholesterol was positively related and **HDL** cholesterol was inversely related to cardiovascular disease mortality. However, multivariable analysis of cardiovascular disease mortality alternately excluding and including **HDL** cholesterol and **LDL** cholesterol as covariates indicated that the effect of alcohol consumption on cardiovascular disease mortality was independent of an **LDL** cholesterol pathway and only partially mediated by an **HDL** cholesterol pathway, while the effect of cigarette **smoking** was independent of both the **HDL** cholesterol and **LDL** cholesterol pathways, suggesting alternative biologic mechanisms of action for both alcohol consumption and cigarette **smoking** on cardiovascular disease.

216: MMWR Morb Mortal Wkly Rep 1987 Sep 4;36 Suppl 4:35S-40S
Some chronic disease risk factors and cigarette smoking in adolescents: the Berlin-Bremen Study.

Dwyer JH, Lippert P, Rieger-Ndakorerwa GE, Semmer NK

Institute for Health Promotion and Disease Prevention Research, University of Southern California, Pasadena 91101.

PM3000457465

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

217: Prev Med 1987 Sep;16(5):647-58

Interdependence of associations of physical activity, smoking, and alcohol and coffee consumption with serum high-density lipoprotein and non-high-density lipoprotein cholesterol--a population study in eastern Finland.

Salonen JT, Happonen P, Salonen R, Korhonen H, Nissinen A, Puska P, Tuomilehto J, Vartiainen E

Department of Community Health, University of Kuopio, Finland.

The interdependence of the associations of physical activity, **smoking**, and consumption of alcohol and coffee with serum high-density lipoprotein and non-high-density lipoprotein cholesterol concentrations was studied in 9,347 persons ages 25-64 years from east and southwest Finland. In covariance analyses with corrections for age, body mass index, saturated fat index, and fasting time, the mean adjusted serum high-density lipoprotein to non-high-density lipoprotein cholesterol ratio was high among physically active male non-smokers but not among smokers (P = 0.024 for two-way interaction). The cholesterol ratio was lower among both men (P = 0.010 for two-way interaction) and women (P = 0.030 for two-way interaction) reporting no or very little use of alcohol, and this association was stronger among smokers and women with high coffee consumption (P less than 0.001 for two-way interaction). Our data suggest that the elevating effect of regular physical exercise on serum high-density lipoprotein cholesterol may be absent in smokers, whereas that of alcohol is greater in smokers than nonsmokers. High coffee consumption associates with decreased serum high-density lipoprotein cholesterol levels in smokers but increased levels in non-smokers.

218: Clin Exp Pharmacol Physiol 1987 Aug;14(8):665-71

Whole blood platelet aggregation is not affected by cigarette smoking but is sex-related.

Taylor RR, Sturm M, Vandongen R, Strophair J, Beilin LJ

Department of Medicine, University of Western Australia, Perth.

1. In normal subjects, 18-49 years old, the effects of the **smoking** habit (greater than 10 cigarettes/day) and the act of **smoking** two cigarettes over 10 min were studied on whole blood platelet aggregation (in vitro impedance method). 2. Acute **smoking** (n = 10) did not affect platelet aggregation to ADP, collagen or to platelet activating factor (PAF) nor thromboxane B2 production during aggregation. There was no difference between smokers (n = 13) and non-smokers (n = 10). However, aggregation to all aggregants was greater in females (n = 11) than males (n = 12) (ADP and collagen, P less than 0.001; PAF, P less than 0.01; ANOVA). 3. Although others have obtained diverse results studying platelet-rich plasma, the absence of an effect of cigarette **smoking** on whole blood platelet aggregation is consistent with many of those observations. Greater in vitro aggregability in females than males is consistent with the few studies of platelet-rich plasma. It seems unlikely that the role of cigarette **smoking** as a risk factor for ischaemic heart disease is related to a direct effect on platelet aggregability.

PM3000457466

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

219: Br Med J (Clin Res Ed) 1987 Jul 25;295(6592):246-7
Impaired intravascular lipolysis with changes in concentrations of high density lipoprotein subclasses in young smokers.

Richmond W, Seviour PW, Teal TK, Elkeles RS

Department of Chemical Pathology, St Mary's Hospital, London.

220: Prostaglandins Leukot Med 1987 Jul;28(2):195-201
Increase in thromboxane B2 and decrease in prostaglandin E2 and 6-keto-prostaglandin F1 alpha release into rat bronchoalveolar fluid as a consequence of cigarette smoking.

Tanizawa H, Iwanaga T, Tai HH

Rats were exposed to cigarette smoke once daily for 4 to 8 weeks. Bronchoalveolar lavage fluid was obtained from each animal and assayed for immunoreactive PGE2, **TXB2** and 6-Keto-PGF1 alpha. Significant increase in **TXB2** and decrease in PGE2 and 6-Keto-PGF1 a release into bronchoalveolar fluid as a consequence of cigarette **smoking** were observed. These changes of arachidonate metabolites in lung alveoli may account in part for bronchoconstriction induced by cigarette **smoking**.

221: Circulation 1987 Jul;76(1):6-14
Biochemical evidence of a chronic abnormality in platelet and vascular function in healthy individuals who smoke cigarettes.

Nowak J, Murray JJ, Oates JA, FitzGerald GA

Cigarette **smoking** is associated with increased mortality from cardiovascular disease that declines after cessation. This study extends the evidence regarding the effects of chronic **smoking** on platelets and the vessel wall in vivo. Excretion of a major urinary thromboxane metabolite, 2,3-dinor-**thromboxane B2**, is significantly (p less than .01) elevated in apparently healthy chronic smokers (20 cigarettes daily) compared with that in non**smoking** control subjects. This difference in excretion of 2,3-dinor-**thromboxane B2** was abolished by the administration of 20 mg aspirin twice daily, a dose shown to selectively inhibit platelet cyclooxygenase. After aspirin, the return of the excretion of 2,3-dinor-**thromboxane B2** to pretreatment levels paralleled the recovery of platelet cyclooxygenase. These findings indicate that excessive thromboxane A2 generation in chronic smokers predominantly derives from platelets. The urinary excretion of the prostacyclin metabolite 2,3-dinor-6-keto-prostaglandin F1 alpha also is increased during chronic cigarette **smoking**, as is the case with other diseases associated with accelerated interaction of platelets with the vessel wall. We have found evidence of platelet and vascular dysfunction in vivo in chronic cigarette smokers before the manifestation of overt cardiovascular disease. The results would also be consistent with the hypothesis that in chronic smokers, the platelet defect is largely reflective of **smoking**-induced vascular injury.

PM3000457467

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

222: Thromb Res 1987 Apr 15;46(2):175-86
Evaluation of platelet function in pregnancy. Comparative studies in non-smokers and smokers.

Davis RB, Leuschen MP, Boyd D, Goodlin RC

We have evaluated the possible role of platelet functional abnormalities as a contributory cause of thrombosis during pregnancy and to the increased fetal mortality and morbidity among women who smoke. Fifty-three pregnant women were enrolled and evaluated on two separate prenatal visits held between the 20th and 36th week of pregnancy and, when possible, post partum. **Smoking** status was evaluated by personal statement and alveolar carbon monoxide levels. Women in the **smoking** group deliberately avoided cigarettes for at least 20 minutes before sampling. Plasma levels of beta-thromboglobulin, thromboxane B2, and 6-Keto PGF1 alpha were evaluated. A significant increase in 6-Keto PGF1 alpha was noted among **smoking** women as pregnancy advanced. 6-Keto PGF1 alpha levels decreased among non-**smoking** women while beta-thromboglobulin increased significantly between the 20th and 33rd week of pregnancy in non-smokers. Platelet aggregation, both in platelet rich plasma and in whole blood (by impedance aggregometry), was evaluated by five different parameters and four different aggregating agents. Significant differences between the non-**smoking** and **smoking** pregnant women were noted for selected age cohorts and aggregating agents. An increase in platelet reactivity among smokers was observed in whole blood by impedance aggregometry with adenosine diphosphate and in two age cohorts using platelet rich plasma. In two groups in which aggregation was significantly accelerated among non-smokers, epinephrine was used as the aggregating agent.

223: Biochim Biophys Acta 1987 Apr 3;918(2):115-9
Selective inhibition of 5-lipoxygenase pathway in rat pulmonary alveolar macrophages by cigarette smoking.

Mobley A, Tanizawa H, Iwanaga T, Tai CL, Tai HH

Pulmonary alveolar macrophages from sham or cigarette-smoke-exposed rats were examined for their ability to transform exogenously added arachidonate to metabolites of lipoxygenase and cyclooxygenase pathways. Synthesis of 5-HETE and leukotriene B4 was selectively inhibited by cigarette smoke exposure, whereas the formation of prostaglandin E2 and thromboxane B2 remained unchanged. Selective inhibition of the lipoxygenase pathway was further reflected by the reduced content of leukotriene B4 in bronchoalveolar fluid of smoke-exposed rats. These results suggest that lipoxygenase-derived products may play a unique role in **smoking**-induced pulmonary diseases.

PM3000457468

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

224: Atherosclerosis 1987 Mar;64(1):71-3
Serum malanodialdehyde (TBA reactive substance) levels in cigarette smokers.

Nadiger HA, Mathew CA, Sadasivudu B

Serum **malanodialdehyde** (MDA) levels in 40 smokers and 23 non-smokers belonging to different age groups were estimated. The MDA levels were high in smokers of all age groups having a history of **smoking** for less than 10 years. MDA levels, however, were not elevated in smokers with a history of **smoking** for more than 10 years. These results are discussed and are interpreted as suggestive that MDA might alter the **LDL** and lead to deposition of cholesterol in arterial wall macrophages explaining thereby the risk of ischaemic heart disease in cigarette smokers.

225: Tohoku J Exp Med 1987 Mar;151(3):261-8
Effects of smoking on regional cerebral blood flow in cerebral vascular disease patients and normal subjects.

Kubota K, Yamaguchi T, Fujiwara T, Matsuzawa T

The chronic effect of **smoking** on the regional cerebral blood flow (r-CBF) was studied by 133-Xenon inhalation method and described with the Initial Slope Index (ISI). Fifty-two patients as the control group who had no abnormality neurologically or with CT scan, 32 patients with old cerebral infarction and 20 patients with old cerebral hemorrhage were introduced to the present study, and these patients were divided into smokers and non-smokers in each group. Those whose **smoking** index of 200 or more [(number of cigarettes/day) X (years of **smoking** history) greater than or equal to 200] were designated as smokers. ISI values were decreased significantly in smokers than non-smokers in all groups. Mean ISI value of unaffected hemisphere in smokers decreased by 16% in the infarction group and 22% in the hemorrhage group comparing to the non-smokers', respectively. In the control group, mean ISI value of right hemisphere decreased by 15% and left 14% in smokers compared to the non-smokers. The r-CBF values in 44 of the 47 smokers were found to be lower than the expected age matched values in non-smokers. Serum **high density lipoprotein** cholesterol value in smokers was significantly lower than that in non-smokers. We demonstrated preliminarily that the **smoking** chronically reduced the r-CBF. Advanced atherosclerosis associated with the smoker was suggested to affect the CBF.

PM3000457469

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

226: Circulation 1987 Jan;75(1):124-30
The association of increased levels of intermediate-density lipoproteins with smoking and with coronary artery disease.

Steiner G, Schwartz L, Shumak S, Poapst M

Studies were undertaken to determine whether there is an association between elevated levels of intermediate-density lipoproteins (IDL) (Sf 12-60 lipoproteins) and coronary artery disease. Forty-five to sixty-five-year-old men with objectively documented coronary artery disease (n = 58) who were free of known risk factors (diabetes, hypertension, obesity, hyperuricemia, and hypercholesterolemia) were compared with similar men who were free of coronary artery disease (n = 52). Smokers could not be excluded. The coronary artery disease group had a higher rate of cigarette **smoking** (NS, due to large variations); higher concentrations of triglycerides in their plasma (p = .003) and higher levels of very low-density lipoproteins (V**LDL**) (p = .007), IDL (p = .016), and low-density lipoproteins (**LDL**) (p = .04); as well as somewhat lower levels of high-density lipoprotein (**HDL**) cholesterol (p = .04). Chi-squared analysis demonstrated a strong association between coronary artery disease and IDL apolipoprotein (apo) B (p = .006), coronary artery disease and IDL triglyceride (p = .032), and coronary artery disease and IDL apo B times IDL triglyceride (p = .006) when the top quintile of the population was compared with the bottom quintile for each of these variables. Stepwise logistic regression analysis resulted in rejection of an association between coronary artery disease and **HDL** cholesterol, plasma triglyceride, V**LDL** triglyceride, or **LDL** triglyceride. However, it did show that coronary artery disease was most strongly associated with **smoking** and that the second strongest association was with IDL.(ABSTRACT TRUNCATED AT 250 WORDS)

227: Prog Clin Biol Res 1987;242:155-63
Thromboxane concentrations in arterial blood of cigarette smokers and hypertensive subjects.

Krause FJ

Department of Radiology, Krankenanstalten des Zollernalbkreises, Kreiskrankenhaus Albstadt, W. Germany.

PM3000457470

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

228: Soz Praventivmed 1987;32(2):69-77
[Cholesterol, arterial pressure and cigarette smoking in the Swiss population: the MONICA project].

[Article in French]

Bernard B, Martin R, Dominique H, Fabrizio B, Gianfranco D, Felix G

Elevated plasma cholesterol, high blood pressure and cigarette **smoking** are three major risk factors for coronary heart disease. Within the framework of Switzerland's participation in the multicenter study MONICA (MONItoring of trends and determinants in CArdiovascular disease), proposed by the WHO, a first risk factor survey was conducted in a representative sample of the population (25-74 years) of two reporting units (cantons of Vaud and Fribourg, canton of Tessin). A high blood cholesterol level (greater than 6,7 mmol/l) is the most common risk factor for coronary heart disease among the studied population. Among men, about 13% have elevated blood pressure, the proportion being about one in ten among women; these proportions increase with age and are slightly above these values in Tessin. Cigarette **smoking** is still a common behavior; between 25 and 45 years one third of the population (male and female) regularly smoke cigarettes.

229: Eur J Haematol 1987 Jan;38(1):55-9
Platelet reactivity, fibrinogen and smoking.

Dotevall A, Kutti J, Teger-Nilsson AC, Wadenvik H, Wilhelmsen L

40 young healthy male volunteers (20 habitual smokers and 20 non-smokers) were investigated with respect to platelet reactivity, plasma **fibrinogen** and coagulation factor VIII. Smokers had significantly lower systolic blood pressures and higher venous platelet counts. The results for ADP-induced platelet aggregation, plasma concentrations for the 2 alpha-granule proteins, beta-thromboglobulin and platelet factor 4, did not differ between the 2 study groups involved; nor was there any difference between serum **thromboxane B2** formation or plasma factor VIII:C activity. However, as compared to non-smokers, plasma **fibrinogen** levels were significantly higher among the smokers.

PM3000457471

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

230: Am J Obstet Gynecol 1986 Dec;155(6):1276-80

Comparative evaluation of antepartum and postpartum platelet function in smokers and nonsmokers.

Leuschen MP, Davis RB, Boyd D, Goodlin RC

Platelet aggregation was analyzed during normal pregnancy by evaluation of the same patient cohort (n = 19) on two separate prenatal visits and at 4 weeks post partum. To analyze platelet aggregation five different parameters were evaluated in platelet-rich plasma and whole blood (by impedance aggregometry) with the use of four different aggregating agents: adenosine diphosphate, collagen, sodium arachidonate, and epinephrine. Plasma levels of beta-thromboglobulin, **thromboxane B2**, and 1,6-keto-prostaglandin F1 alpha were also analyzed. Platelet counts rose 19% after delivery. Plasma levels of beta-thromboglobulin and **thromboxane B2** were not significantly changed during the two antepartum visits, but B-thromboglobulin levels were modestly elevated post partum. Levels of 1,6-keto-prostaglandin F1 alpha decreased significantly from a mean of 125 pg/ml before delivery to 50 pg/ml post partum. All antepartum parameters on whole blood aggregation that were significantly different from postpartum values showed enhanced antepartum reactivity. In platelet-rich plasma, pregnancy was associated with greater platelet reactivity except for two variables, time to half-maximal aggregation for epinephrine and the extent of aggregation by collagen, both noted during the first antepartum evaluation. When the patient cohort of 19 was subdivided according to **smoking** status, all aggregation parameters of significance (p less than 0.05) demonstrated increased platelet reactivity during pregnancy compared with postpartum values. **Smoking** women accounted for a disproportionate number of significantly enhanced reactivity (seven variables versus three).

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

231: Thromb Res 1986 Oct 1;44(1):85-94
Cigarette smoking and platelet function.

Marasini B, Biondi ML, Barbesti S, Zatta G, Agostoni A

To assess the influence of cigarette **smoking** on platelet activation, we studied the changes in intraplatelet and platelet-released serotonin (5-HT) and plasma levels and platelet-associated production of thromboxane B2 (**TXB2**), in 6 non smokers and 6 habitual smokers, before and after acute exposure to smoke. Before **smoking**, habitual smokers showed slightly higher, albeit not significantly, 5-HT platelet concentrations and **TXB2** plasma levels, as well as lower **TXB2** platelet production after collagen and even more after ADP stimulation (0.59 +/- 0.27 vs 1.35 +/- 0.46 and 0.99 +/- 0.47 vs 2.08 +/- 0.51 ng/10(8) platelets for habitual smokers vs controls, 4 and 10 min after ADP, p less than 0.02). No significant differences in platelet 5-HT release were observed. Acute **smoking** did not induce any significant change from baseline in either 5-HT or **TXB2** for controls, while significantly reduced **TXB2** production from ADP-challenged platelets from habitual smokers (0.30 +/- 0.15 vs 0.59 +/- 0.27 ng/10(8) platelets, immediately after **smoking** vs baseline, p less than 0.01). Ninety min after the completion of the **smoking**, the values had returned to baseline. Immediately after **smoking**, significant differences were found between habitual smokers and controls for **TXB2** platelet production (2.76 +/- 1.78 vs 6.42 +/- 1.60, p less than 0.025 and 3.01 +/- 1.90 vs 6.44 +/- 2.26 ng/10(8) platelets, p less than 0.05, for habitual smokers vs controls, 4 and 10 min after the addition of collagen; 0.30 +/- 0.15 vs 1.20 +/- 0.84 and 0.79 +/- 0.50 vs 1.70 +/- 0.74 ng/10(8) platelets, p less than 0.05, after ADP stimulation). Differences were no longer significant 90 min after **smoking**. Our data indicate that cigarette **smoking** is associated with platelet dysfunction, which seems due to impairment of metabolic platelet capacity rather than increased platelet activation in vivo.

232: Am J Epidemiol 1986 Oct;124(4):706-10
Changes in plasma high density lipoprotein cholesterol after changes in cigarette use.

Fortmann SP, Haskell WL, Williams PT

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

233: Atherosclerosis 1986 Aug;61(2):149-54
The effect of age, sex, alcohol consumption and cigarette smoking on serum concentrations of lipids and apolipoproteins in Zimbabwean blacks.

Gomo ZA

Serum concentrations of total cholesterol, **HDL** cholesterol, triglycerides and apolipoproteins A-I and B were studied in black subjects with no known risk factor for coronary heart disease and in subjects with a single risk factor. The concentrations of lipids and apolipoproteins were sex-dependent. **HDL** cholesterol and apolipoprotein A-I were age-dependent in females (P less than 0.05 and P less than 0.01, respectively). There was a dose-related association between alcohol consumption and serum concentrations of triglycerides, **HDL** cholesterol, apolipoproteins A-I and B in males (P less than 0.001 and P less than 0.002, respectively in the heavy drinkers). The effects of cigarette **smoking** on the concentrations of serum lipids and apolipoproteins appear to be prominent in the heavy **smoking** subjects (P less than 0.001 and P less than 0.001, respectively). This work suggests that **HDL** cholesterol and apolipoprotein A-I may discriminate black subjects at risk of developing atherosclerosis.

234: Atherosclerosis 1986 Jun;60(3):287-90
Effects of smoking on lipid parameters during therapeutic weight loss.

Van Gaal LF, De Leeuw IH

Evaluation of the obesity- and **smoking**-related atherogenic risk in an obese population, was studied by retrospectively reporting the 6-month dietary effect on metabolic lipoprotein parameters. In a non-smoker group, a weight reduction programme exhibits a marked improvement (P less than 0.05) of **HDL** and **LDL** cholesterol and atherogenic index. **Smoking** during successful, therapeutic weight reduction inhibits this advantageous improvement of lipid parameters, especially in women. In regard to the lipoprotein related vascular risk, obesity treatment without modifying **smoking** habits is less advantageous.

235: J Vasc Surg 1986 May;3(5):807-12
On the arterial consequences of smoking.

Couch NP

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236: Am J Clin Nutr 1986 Apr;43(4):486-94
Effects of smoking cessation on weight gain, metabolic rate, caloric consumption, and blood lipids.

Stamford BA, Matter S, Fell RD, Papanek P

Thirteen sedentary adult females successfully quit **smoking** cigarettes for 48 days. Mean daily caloric consumption increased 227 kcal and mean weight gain was 2.2 kg. There were no measurable acute effects of smoke inhalation and no chronic net effects of **smoking** cessation on resting metabolic rate, as determined by oxygen consumption and respiratory exchange ratio. After 1 yr, subjects who continued to abstain gained an average of 8.2 kg. **HDL**-cholesterol increased 7 mg/dl in 48 days; however, this effect was lost in those who returned to **smoking**. Increased caloric consumption accounted for 69% of weight gained immediately following **smoking** cessation. Factors other than changes in caloric consumption and metabolic rate may be responsible for a significant proportion (31%) of the weight gained in individuals who quit **smoking**

237: Acta Med Scand 1986;219(2):167-71
Distribution of high density lipoprotein cholesterol according to relative body weight, cigarette smoking and leisure time physical activity. The Cardiovascular Disease Study in Finnmark 1977.

Forde OH, Thelle DS, Arnesen E, Mjos OD

The relationship between **HDL** cholesterol and relative body weight, cigarette **smoking** and leisure time physical activity were examined in 7338 healthy men and 6768 healthy women aged 20-53 years, living in Finnmark County, Northern Norway. The independent effects of the three factors were examined by an analysis of covariance. In both sexes a strong and almost linear negative association was observed between relative body weight and **HDL** cholesterol. **HDL** cholesterol was lower in smokers than in non-smokers, the difference being more pronounced in females than in males. A weak but significant positive association was observed between leisure time physical activity and **HDL** cholesterol in both sexes.

238: Monogr Atheroscler 1986;14:40-2
The prospective intervention study Eberbach-Wiesloch--influence of **smoking**.

Schettler G, Buchholz L, Gnasso A, Haberbosch W, Kostner G, Morgenstern W, Nussel E, Augustin J

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Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

239: Prev Med 1986 Jan;15(1):35-45
Effects of smoking and stopping smoking on serum high-density lipoprotein cholesterol levels in a representative population sample.

Tuomilehto J, Tanskanen A, Salonen JT, Nissinen A, Koskela K
Serum high-density lipoprotein (**HDL**) cholesterol levels were assessed in a random sample of 939 men and 853 women ages 14-65 years in eastern Finland. Amount of daily **smoking** measured by serum thiocyanate concentration was negatively and independently associated with serum **HDL** cholesterol level and **HDL**/total cholesterol ratio in men. This negative association seemed largely to be due to low **HDL** cholesterol levels in heavy smokers. Both male and female current smokers had lower **HDL** cholesterol levels and **HDL**/total cholesterol ratios than those who had never smoked. This difference was found even after adjustment for age, body mass index, and beer drinking. The reduction of **HDL** cholesterol level seemed to be reversible, because those who had recently stopped **smoking** had higher **HDL** cholesterol levels and higher **HDL**/total cholesterol ratios than current smokers.

240: Arch Toxicol Suppl 1986;9:120-3
Cigarette smoking, serum lipids and angiographically-assessed coronary artery disease.

Thevenin M, Barcellos GA, Dumont G

Seventy-six patients underwent cardiac catheterization for evaluation of suspected coronary artery disease and their serum lipid fractions and cigarette **smoking** habits were evaluated in order to determine the incidence of these risk factors on coronary artery disease. Results showed that patients with angiography defined coronary artery disease (CAD) presented disturbances in their serum lipid fractions, especially **LDL**-cholesterol, apoprotein B and the ratio **HDL**-C/(TC-**HDL**-C). Coronary lesions from smokers were higher when compared with matched non smokers with CAD. Cessation of **smoking** for two years did not induce regression of CAD among past smokers.

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241: Atherosclerosis 1985 Dec;58(1-3):17-25
Variation in serum lipid and lipoprotein levels associated with changes in smoking behaviour in non-obese Caucasian males.

Shennan NM, Seed M, Wynn V

A population of healthy male caucasians was analysed with respect to lipid and lipoprotein parameters, according to differences in current and previous **smoking** patterns. High density lipoprotein (**HDL**) cholesterol, and the **HDL**2 subfraction were significantly higher in non-smokers compared to current smokers. In ex-smokers, the levels of these 2 parameters increased with the length of time since giving up the habit, until levels were no longer distinguishable from non-smokers. A similar increase was observed for weight, although both triglyceride and very low density lipoprotein (V**LDL**) levels decreased. Low density lipoprotein (**LDL**) levels showed no significant variation in any of the comparisons. Lower alcohol consumption in both the ex-smokers, and in the non-smokers may account partially for the changes in triglyceride and V**LDL**, although the same observation is contrary to the effects observed in both **HDL** and **HDL**2.

242: Eur Heart J 1985 Dec;6(12):1063-8
Acute influence of cigarette smoke in platelets, catecholamines and neurophysins in the normal conditions of daily life.

de Lorgeril M, Reinharz A, Busslinger B, Reber G, Righetti A

Cigarette **smoking** is firmly linked to the occurrence of acute coronary events. In twenty-two healthy volunteers in normal conditions of daily life we studied the acute influence of **smoking** on the following parameters: beta-thromboglobulin, thromboxane B2, epinephrine, norepinephrine, estrogen-stimulated neurophysin, and nicotine-stimulated-neurophysin. Our results show that in our population and following our protocol, **smoking** did not induce platelet activation, thromboxane formation, catecholamine release or estrogen-stimulated-neurophysin secretion. However, **smoking** did provoke a significant increase of nicotine-stimulated-neurophysin (p less than 0.05) which reflects vasopressin increase and which might explain the high incidence of ischaemic accidents in cigarette **smoking** via the vasoactive properties of vasopressin.

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Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

243: Circulation 1985 Nov;72(5):971-4
The relationship of white cell count, platelet count, and hematocrit to cigarette smoking in adolescents: the Oslo Youth Study.

Tell GS, Grimm RH Jr, Vellar OD, Theodorsen L

This article reports on the relationship between cigarette **smoking**, white blood cell count (WBC), platelet count (PC), and hematocrit in a Norwegian adolescent population. Data were obtained on 439 youths, 14 to 16 years old, as part of the Oslo Youth Study, an investigation of risk factors and behaviors for cardiovascular disease and cancer among adolescents. Analyses of covariance, controlling for height, weight, age, sexual maturation, high-density lipoprotein (**HDL**) cholesterol, and hematocrit revealed that both male and female regular smokers (those reporting **smoking** at least once a week) had significantly higher mean WBCs. Male regular smokers also had significantly higher PCs than nonsmokers, and female regular smokers had higher PCs than young women who smoked less often than once a month. Hematocrit, after adjustment for height, weight, age, sexual maturation, and **HDL** cholesterol, was significantly lower in male regular smokers, while female regular smokers had higher hematocrit values than nonsmokers or occasional smokers. Results of this study show that WBC and PC were increased in adolescents who started **smoking** relatively recently. This indicates that the increase in white cell count observed in smokers is unlikely to be due to a longstanding **smoking**-induced chronic disease condition.

244: Atherosclerosis 1985 Nov;57(2-3):343-6
Lipid levels in high density lipoprotein subfractions in smokers with peripheral vascular disease.

Dionyssiou-Asteriou A, Kalofoutis A

No significant difference in **HDL** cholesterol was found between smokers with PVD and corresponding controls. The ratio of **HDL** cholesterol to the sum of (V**LDL** + **LDL**) cholesterol was reduced in patients with PVD. Patients with PVD had significantly highly serum triglyceride levels. A slightly significant difference could be demonstrated for serum cholesterol and serum phospholipids concentrations in **smoking** patients with PVD.

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245: Prostaglandins Leukot Med 1985 Aug;19(2):167-76
Aggregation of and thromboxane B2 synthesis in platelets from newborn infants of smoking and non-smoking mothers.

Ahlsten G, Ewald U, Kindahl H, Tuvemo T

Cord blood platelet aggregation and thromboxane B2 (**TxB2**) synthesis were investigated in 20 healthy infants of drug-free healthy mothers with an uncomplicated pregnancy ending at term in a normal vaginal delivery. Eight of the mothers were habitual smokers and the remaining 12 were non-smokers. The platelet count was slightly lower in infants of **smoking** mothers than in the control infants. There were no differences between the two groups in the qualitative or quantitative aggregation responses (maximal change in optical density) to stimulation by 0.55, 1.1, 3.3 and 6.6 microM adenosine diphosphate, 0.5 and 1.0 mM arachidonic acid (AA) or collagen 1.0 and 5.5 mg/l. Nor was there any difference between the groups in regard to **TxB2** synthesis after stimulation by these substances. The amount of **TxB2** synthesized merely reflected the occurrence of reversible or irreversible platelet aggregation. Stimulation of platelets by AA induced by far the highest synthesis of **TxB2**. The generally decreased aggregability of platelets of newborn infants, compared with that in adults, was confirmed in this study. No effect of maternal **smoking** during pregnancy on the prostaglandin-dependent pathway of aggregation of cord blood platelets was demonstrated.

246: Vnitr Lek 1985 Jul;31(7):700-5
[Physical activity, smoking and obesity in relation to HDL-cholesterol in 18-year-olds].

[Article in Slovak]

Baloga S, Brtkova M

247: Aviat Space Environ Med 1985 Jul;56(7):709-13
HDL-cholesterol related to weight, smoking, and physical fitness in German Air Force pilots.

Reichenbach-Klinke K, Koch S, Burchard EC

This study was undertaken to find out the importance of **HDL**-cholesterol in assessing coronary risk in our pilots. We related cholesterol, **HDL**-cholesterol, and the cholesterol/**HDL**-cholesterol ratio in blood to the BROCA-Index, **smoking**, and relative PWC 150 in 589 individuals. We found positive correlations between the cholesterol/**HDL**-cholesterol ratio to the BROCA-Index and to **smoking**. We did not find any correlation between cholesterol alone and the BROCA-Index or **smoking**. Moreover, we failed to find any correlations to physical fitness calculated from PWC 150. That may be due to the higher physical fitness standard in our pilots in comparison with the normal population. It is concluded, that a **HDL**-cholesterol determination is a more relevant parameter than cholesterol alone in borderline and elevated cholesterol levels.

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248: G Ital Med Lav 1985 Jul;7(4):119-25
Serum lipids and lipoproteins in relation to smoking among the apparently healthy workers: a preliminary survey. The Pavia Study.

Pollini G, Maugeri U, Tringali S, Jedrychowski W

This pilot study is concerned mainly with the interrelationships between serum lipids and lipoproteins, and personal variables like age, body mass index (BMI) and **smoking** habit. The analysis was limited to the male workers employed in the Lombardia region. The results of the study confirm the findings of the other investigators on the interaction between **smoking** and lipid metabolism. The effect of **smoking** on the cholesterol level appeared to have been the most pronounced and the clear strong relationship with the exposure was established. Also triglycerides concentration was related to the **smoking** exposure. The **HDL** lipoproteins were lower and **LDL**-**VLDL** higher in smokers than in nonsmokers, however, the association with the **smoking** exposure was insignificant. The findings showed that **HDL**-cholesterol level was inversely dependent on the plasma triglycerides both in nonsmokers and smokers. The paper discusses the implications of the research carried out on the interpretation of the **HDL**-cholesterol values as a eventual potential risk factor for the coronary heart disease.

249: Thromb Haemost 1985 Jun 24;53(3):419-22
Platelet thromboxane formation and bleeding time is influenced by ethanol withdrawal but not by cigarette smoking.

Hillbom M, Muuronen A, Lowbeer C, Anggard E, Beving H, Kangasaho M

Platelet count, mean volume, aggregation and associated thromboxane (**TXB2**) formation, circulating platelet aggregates and bleeding time were examined in 19 noncirrhotic male alcoholic cigarette smokers for four weeks following cessation of prolonged heavy drinking, and in 24 nonalcoholic healthy male volunteers (10 smokers and 14 nonsmokers). The alcoholics showed a 9-fold increase (p less than 0.001) in ADP-stimulated platelet thromboxane formation one to two weeks after ethanol withdrawal. The effect was transient and coincided with a significant (p less than 0.01) shortening of skin bleeding time and a slight increase in circulating platelet aggregates suggesting proneness to thrombosis. No differences were seen between the **smoking** and non**smoking** healthy volunteers. We conclude that the recovery phase after prolonged heavy drinking is characterized by a transient increase in platelet reactivity which may lead to increased spontaneous formation of circulating platelet aggregates and shortening of bleeding time.

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250: JAMA 1985 May 24-31;253(20):2965-9
Myocardial infarction and cigarette smoking in women younger than 50 years of age.

Rosenberg L, Kaufman DW, Helmrich SP, Miller DR, Stolley PD, Shapiro S

The modifying influence of individual risk factors on the relation between myocardial infarction (MI) and cigarette **smoking** was evaluated in a case-control study of women younger than 50 years of age. Data from 555 women who survived first MIs were compared with those of 1,864 hospital controls of similar ages. The risk of MI increased with the number of cigarettes smoked, both in the presence and absence of factors that predispose to an infarction. In particular, the association was apparent at all ages, at all levels of total serum cholesterol and high-density lipoprotein cholesterol, and in the presence and absence of oral contraceptive use, hypertension, diabetes mellitus, blood group A, tendency to type A behavior, and family history of MI. The relative increase in risk was generally greater the lower the underlying predisposition to MI. There was clear evidence, however, that recent oral contraceptive use substantially augmented the increased risk for smokers, and hypercholesterolemia may have had the same effect.

251: Nippon Ronen Igakkai Zasshi 1985 May;22(3):245-50
[Effects of smoking on brain aging. I. Cerebral blood flow and smoking--a study with the 133-xenon inhalation method].

[Article in Japanese]

Kubota K, Matsuzawa T, Yamaguchi T, Fujiwara T, Seo S, Sasaki Y

252: Riv Neurol 1985 Mar-Apr;55(2):88-98
[Smoking and acute cerebrovascular disorders of the ischemic type].

[Article in Italian]

Cazzato G, Zorzon M, Monti F, Camerotto A

In order to define the relationships between cigarette **smoking** and occurrence of cerebrovascular disease, a retrospective study was undertaken regarding **smoking** habits of 187 patients (129 men and 58 women) with cerebral infarct of non-embolic origin and 85 patients (40 men and 45 women) with TIA (transient ischemic attacks). Each patient was matched with a control subject, of the same sex and age group, who showed no signs or symptoms of cerebrovascular disease. Results show a statistically significant association between **smoking** habits and cerebral infarcts only in male subjects who smoked more than 20 cigarettes a day.

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253: Cardiovasc Res 1985 Mar;19(3):155-9
Effect of smoking and dietary saturated fats on platelet functions in Scottish farmers.

Renaud S, Dumont E, Baudier F, Ortchanian E, Symington IS

Coagulation and platelet aggregation to thrombin and adrenaline, before and 10 min after **smoking** one high nicotine cigarette, were studied in 40 healthy male farmers (40 to 45 years) from the South-West and North-East of Scotland. These tests were conducted in association with detailed dietary studies. In the West group the intake of dairy fats, saturated fats and P/S ratio as well as most of the platelet function tests estimated were significantly higher than in the East group. Serum cholesterol (total and **HDL**) was similar in the two regions, while triglycerides were lower in the West. **Smoking** one cigarette considerably enhanced the platelet functions in both areas but the increases were more marked in the West group. The increase in the response of platelets to **smoking** was additive to that apparently induced by the intake of saturated fat in such a way the response of platelets to thrombin and epinephrine after **smoking** one cigarette in the West was approximately four times this obtained before **smoking** (or in a non-smoker) in the East. These additive effects of cigarette and saturated fat might be relevant to the reported higher incidence of coronary heart disease in the West of Scotland.

254: Atherosclerosis 1985 Mar;54(3):241-9
Aberrations in lipoprotein lipids in men with coronary artery disease and the influence of obesity, smoking and beta-adrenoceptor blocking drugs.

Wallentin L, Sundin B

In this study 74 men, 40-60 years old, with incapacitating angina pectoris and angiographically verified coronary artery disease (CAD) were compared to an equal number of randomly sampled healthy men matched for age, occupation and place of living. Obesity and **smoking** were more common in patients than in controls. The patients had elevated cholesterol (C), triglycerides (TG), and phospholipid (PL) levels dependent on raised concentrations of these lipids in the **VLDL** and **LDL**. The C and PL levels in the **HDL** fraction were decreased. Obesity had a significant influence on the **VLDL** and **HDL** levels. Also after taking this influence into account, the CAD patients had higher **VLDL** and **LDL** levels and a lower **HDL** concentration than the controls. Furthermore, regardless of the influence of the TG concentration, the **HDL** level was reduced in the patients. **Smoking** habits had no significant influence on the lipoprotein levels. Treatment with beta-adrenoceptor blocking drugs was not associated with any significant alteration of the **VLDL** or the **HDL** level. The results strengthen the importance of lipoprotein aberrations as risk factors for coronary heart disease also if observed in association with obesity, **smoking** and treatment with beta-adrenoceptor blocking drugs.

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255: Artery 1985;13(1):7-18
Plasma HDL cholesterol and the subclasses HDL2 and HDL3 in smokers and non-smokers.

Nesje LA, Mjos OD

Plasma cholesterol, **HDL** cholesterol, **HDL**2 cholesterol, **HDL**3 cholesterol and triglycerides were examined in 45 healthy males aged 40 to 49 years, living in Finnmark, Northern Norway. In 14 men who had been **smoking** more than 15 cigarettes daily for at least 10 years, **HDL** cholesterol, **HDL**2 cholesterol and **HDL**3 cholesterol were all found to be significantly lower than in 23 non-smokers. No significant difference was found between smokers and non-smokers concerning triglycerides and (total) cholesterol. It is suggested that cigarette **smoking** may promote atherosclerosis by lowering the antiatherogenic subclass **HDL**2.

256: Nihon Kyobu Shikkan Gakkai Zasshi 1984 Dec;22(12):1122-6
[Cigarette smoking and lung metabolism--effect of cigarette smoking on blood levels of 6-keto PGF1 alpha, thromboxane B2 and lipoperoxide in healthy volunteers].
[Article in Japanese]

Ishihara Y, Kitamura S, Chijimatsu Y, Homma H

257: J Am Coll Cardiol 1984 Nov;4(5):964-71
Acute systemic and coronary hemodynamic and serologic responses to cigarette smoking in long-term smokers with atherosclerotic coronary artery disease.

Nicod P, Rehr R, Winniford MD, Campbell WB, Firth BG, Hillis LD

Previous studies suggested that cigarette **smoking** 1) inhibits an increase in coronary blood flow that should occur with increased myocardial oxygen demands, and 2) alters thromboxane and prostacyclin production, causing vasoconstriction and platelet aggregation. In 38 smokers (26 men and 12 women, aged 50 +/- 8 years [mean +/- standard deviation]) with coronary artery disease, systemic and coronary hemodynamic and serologic variables were measured before and after **smoking** two cigarettes (in 8 to 10 minutes) (21 patients) or 8 to 10 minutes without **smoking** (17 patients; control group). No variable changed in the control group. **Smoking** increased (p less than 0.05) heart rate-systolic pressure product, cardiac output and maximal first derivative of left ventricular pressure (dP/dt) without significantly changing the coronary sinus concentrations of thromboxane B2 or 6-keto-prostaglandin F1 alpha (the stable metabolites of thromboxane A2 and prostacyclin, respectively). **Smoking** did not increase coronary flow in 6 of 11 patients with greater than 70% stenosis of the proximal left anterior descending or circumflex coronary artery, or both, whereas it caused an increase in coronary flow in all 10 patients without proximal stenoses (p = 0.006). To determine if **smoking** altered the response of coronary flow to increased myocardial oxygen demands, 10 smokers (5 men and 5 women, aged 48 +/- 9 years) underwent atrial pacing for 5 minutes followed 15 minutes later by atrial pacing for 5 minutes during **smoking**. In the five patients without proximal left coronary artery stenoses, coronary flow increased 26 +/- 29 ml/min with pacing and 45 +/- 21 ml/min with pacing/**smoking** (p =0.018)

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258: Clin Exp Pharmacol Physiol 1984 Nov-Dec;11(6):611-9
The measurement of plasma thromboxane B2 and the effect of smoking.

Sturm M, Barden A, Beilin LJ, Taylor RR

Plasma thromboxane B2 (**TxB2**) was measured by radioimmunoassay using an iodinated ligand following extraction and further purification by thin layer chromatography. Venous blood was sampled into a syringe containing the cyclooxygenase inhibitor meclofenamate. Normal levels, 15 pg/ml (s.d. = 8, n = 21), were lower than usually reported and measured values increased several fold over 20 min sampling from an indwelling needle. With appropriate sampling there was a statistically insignificant increase in plasma **TxB2** after subjects smoked two cigarettes (n = 11). An average decrease occurred in a control group (n = 10) and the difference between groups was of borderline significance (P less than 0.05). **Smoking** did not change **TxB2** production associated with platelet aggregation induced in vitro by collagen, whereas plasma adrenaline increased significantly. The results emphasize the importance of the technique of sampling and assay in the measurement of plasma **TxB2**.

259: Atherosclerosis 1984 Nov;53(2):173-84
Effect of cigarette smoking cessation on risk factors for coronary atherosclerosis. A control clinical trial.

Rabkin SW

The effect of cigarette **smoking** on other cardiovascular risk factors, serum lipids, body weight, blood pressure and blood sugar was assessed in a randomized control trial of reduction or cessation of cigarette **smoking**. In the intervention group (n = 107), reported cigarette use fell from 28.5 +/- 1.2 (+/- SEM) to 10.6 +/- 1.2 cigarettes/day and serum thiocyanate, a biochemical indicator of the extent of tobacco exposure, decreased -42.8 +/- 5.5 mumol/l (P less than 0.001). Compared to the control group, the intervention group showed significant (P less than 0.05) decreases in reported cigarette consumption and serum thiocyanate and significant (P less than 0.05) increases in body weight and skinfold thickness. Change in thiocyanate correlated significantly (P less than 0.05) and inversely with change in **HDL**-C, body weight and skinfold thickness, but not with change in **LDL**-C, triglycerides or blood pressure. These relationships remained significant even after adjusting in multivariate analysis, for initial measurements of these variables or regression to the mean. For those who quit **smoking** (n = 35) **HDL**-C increased 5.9 +/- 1.7 mg/dl (P less than 0.01). The usual inverse relationship between body weight and **HDL**-C does not exist with cessation of cigarette **smoking**. Thus, benefits of stopping cigarette **smoking** extend to favourable alterations in **HDL**-C and there are no adverse effects on blood pressure, fasting blood sugar, triglycerides or **LDL**-C.
Clinical trial
Controlled clinical trial

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260: Atherosclerosis 1984 Jul;52(1):73-83
Cigarette smoking, exercise and high density lipoprotein cholesterol.

Stamford BA, Matter S, Fell RD, Sady S, Papanek P, Cresanta M

Cigarette **smoking** is associated with depressed levels of **HDL**-C, whereas exercise is associated with elevated levels of **HDL**-C. The purpose was to determine effects of **smoking** and exercise on blood lipids and lipoproteins in middle-aged males. It was hypothesized that **smoking** may attenuate the effects of exercise to elevate **HDL**-C. A total of 269 males (70 smokers) met all criteria for inclusion in the study population. Age, height, weight, body fatness via hydrostatic weighing, daily caloric consumption and alcohol intake, and **smoking** habits and history were determined. Interviews concerning physical activity patterns were conducted and cardiovascular responses to treadmill exercise were determined. Subjects were grouped as sedentary (low activity), participants in vigorous recreational activities (moderate activity) and joggers/runners (high activity). Analysis of covariance with adjustments for factors which may affect blood lipids and lipoproteins was employed. Smokers demonstrated lower **HDL**-C and higher total cholesterol levels than nonsmokers. High activity subjects demonstrated significantly higher **HDL**-C levels than the low and moderate groups which did not differ. High activity smokers did not differ from low activity nonsmokers with respect to **HDL**-C. This supports the proposed hypothesis. Nonsmokers were higher in weight and body fatness than smokers even though smokers consumed 288 more calories per day on the average. This suggests that **smoking** may account for a significant number of calories through altered metabolism or some other means.

261: Int J Epidemiol 1984 Jun;13(2):177-83
Smoking status and lipid levels in adults of different ethnic origins: the Jerusalem Lipid Research Clinic Program.

Halfon ST, Green MS, Heiss G

Jerusalem Lipid Research Clinic Program. International Journal of Epidermiology 1984; 13: 177-183. The relationship between cigarette **smoking** and plasma lipids and lipoproteins was examined in a random sample of 1115 male and 563 female adult participants in the Jerusalem Lipid Research Clinics Program. Differences in plasma lipids and lipoproteins, cigarette **smoking**, alcohol consumption, and body mass index were demonstrated between the four country of origin groups in both sexes. Using multiple linear regression analysis, an inverse association was shown between **smoking** and **HDL** cholesterol, significant only in females (p less than 0.001). Potential confounding variables-Quetelet's index of body mass, alcohol consumption, age, and country of origin groups-revealed only a weak effect on the **smoking**-**HDL**-cholesterol association. Examination of an interaction between origin group and **smoking** showed the same **smoking**-lipid level association in each of the four country of origin groups, and in both sexes. A strong association was found between **smoking** and **LDL**-cholesterol only in females (p less than 0.01). Triglycerides and **VLDL**-cholesterol showed a weak association with **smoking** in this study.

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262: J Clin Chem Clin Biochem 1984 Jun;22(6):397-402
The effects of cigarette smoking on serum levels of HDL cholesterol and HDL apolipoprotein A-I. Findings of a prospective epidemiological study on employees of several companies in Westphalia, West Germany.

Assmann G, Schulte H, Schriewer H

In preventive studies of company employees in Westphalia, **HDL** cholesterol was measured in the sera of 4933 men and 2365 women, as well as **HDL** apolipoprotein A-I in the sera of 3509 men and 1648 women. Three subgroups were compared: non-smokers = persons who have never smoked; ex-smokers = persons who do not smoke at present but did in the past; smokers = persons who smoke cigarettes at present. Mean values for **HDL** cholesterol and for **HDL** apolipoprotein A-I were significantly lower in smokers than in non-smokers or in ex-smokers, while there were no differences between the last two groups. These differences appeared in both sexes but were more pronounced in women than in men. To answer the question whether the observed differences are caused by the consumption of cigarettes by itself or whether they are caused by the presence of other risk factors, further subgroups were compared to assess the influence of the risk factors obesity, hypertension, hypercholesterolaemia, hyperglycaemia and hyperuricaemia. It was found that - regardless of the presence of no, one, two or more risk factors - the frequency of probands with low **HDL** cholesterol values (less than 0.907 mmol/l (men); less than 1.166 mmol/l (women] was about 10% higher in smokers than in non-smokers or ex-smokers. Subgroups based on the number of risk factors did not exhibit the same clear distribution for apolipoprotein A-I values as were seen for **HDL** cholesterol. The results are interpreted in the light of the existing literature.

263: Adv Exp Med Biol 1984;164:339-57
Platelet activity in relation to smoke and exercise in patients with chronic obstructive lung disease: effects of platelet antiaggregating drugs.

Novo S, Davi G, Caimi G, Castello F, Valdes L, Marino S, Romano A, Fazio M, La Menza B, Mazzola A, et al

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

264: Klin Wochenschr 1984;62 Suppl 2:36-42
Acute influence of smoking on plasma lipoproteins.

Gnasso A, Haberbosch W, Schettler G, Schmitz G, Augustin J

This study was designed to investigate acute effects of **smoking** on plasma lipoproteins. Twelve fasting smokers inhaled the smoke of two cigarettes. Blood samples were taken before and 30 min after **smoking**. Triglycerides decreased in plasma from 136.8 +/- 39.8 to 108.0 +/- 34.9, in **VLDL** from 79.8 +/- 31.4 to 58.4 +/- 28.5 mg%. Cholesterol fell in **HDL**3 from 29.9 +/- 5.0 to 26.6 +/- 5.8 mg%. Determination of **HDL**-cholesterol with the phosphotungstic acid precipitation method revealed a reduction from 45.7 +/- 10.2 to 40.3 +/- 11.1 mg% after **smoking**. All C-apoproteins decreased in **VLDL** as an entity. Apoprotein A-I was diminished in plasma from 137.5 +/- 23.1 to 118.2 +/- 25.4, and in **HDL**3, from 97.1 +/- 12.1 to 85.0 +/- 13.1, apoprotein A-II in plasma from 28.6 +/- 8.9 to 24.7 +/- 6.9 and in **HDL**3 from 21.1 +/- 8.4 to 17.4 +/- 5.7 mg%. Zonal ultracentrifugation of D less than 1.063 g/ml lipoproteins confirmed the influence of **smoking** on **VLDL**. In **LDL**, an increase in cholesterol esters, mainly cholesterol linoleate, from 57.3 +/- 30.2 to 67.4 +/- 25.9 mg% was observed after **smoking**. The **HDL**2 subclass was shifted toward a slightly lighter hydrated density, but the major effect of **smoking** was seen in **HDL**3. Total cholesterol decreased from 30.5 +/- 7.3 to 22.3 +/- 6.6 mg%, due to a fall of all major cholesterol esters from 23.7 +/- 7.2 to 15.8 +/- 6.9 mg%. **HDL**3-phospholipids were reduced from 74.9 +/- 37.0 to 46.0 +/- 23.9 mg%.(ABSTRACT TRUNCATED AT 250 WORDS)

265: Klin Wochenschr 1984;62 Suppl 2:32-5
HDL phosphatidyl choline and cigarette **smoking**.

Assmann G, Schulte H, Schriewer H

The influence of cigarette **smoking** on the concentration of **HDL** phosphatidyl choline was tested in 1,546 male and 778 female employees in Westfalia, and the results were compared with the influence of cigarette **smoking** on the concentration of **HDL** cholesterol. Three subgroups were established for comparison: non-smokers = persons who had never smoked; ex-smokers = persons who had in the past been smokers but were now non-smokers; and smokers = persons who at present smoked cigarettes. Neither male nor female smokers proved to have different **HDL** phosphatidyl choline values when compared to non-smokers or ex-smokers, whereas male and female smokers were found to have decreased **HDL** cholesterol values when compared to non-smokers (p less than 0.01) or ex-smokers (p less than 0.05). In female smokers a correlation was found between **HDL** phosphatidyl choline values and the number of cigarettes smoked every day (r = -0.12, p less than 0.05).

PM3000457487

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

266: Klin Wochenschr 1984;62 Suppl 2:18-27
Influence of smoking on the plasma lipoprotein profile.

Seidel D, Cremer P, Elster H, Weise M, Wieland H

Smoking and hypercholesterolemia, or more specifically hyper-beta-lipoproteinemia, are well established risk factors for the early development of atherosclerotic disease. The presence of both factors augments the potential risk. The question arises, therefore, as to whether cigarette **smoking** has a direct effect on the plasma lipoproteins and, in particular, on the atherogenetic low density lipoproteins. In this study, the influence of cigarette **smoking** on the lipoprotein profile was investigated in a defined cohort of 6,543 male industrial workers aged 40-59 years, consisting of 2,434 smokers and 3,975 non-smokers. The effect of **smoking** on the lipoprotein profile showed no significant changes in **LDL** and only slight changes in the other lipoprotein fractions. Other factors, such as alcohol intake, body weight, and general life style seem to have a greater influence on **HDL**-cholesterol than **smoking**. It is concluded that **smoking** does not significantly alter lipid metabolism and that minor differences observed between smokers and non-smokers are due to a variety of factors, rather than a reflection of a direct metabolic relationship.

267: Prostaglandins Leukot Med 1983 Dec;12(4):439-42
Cigarette smoke ventilation decreases thromboxane B2 metabolism in isolated rat lungs.

Mannisto J, Uotila P

3H-**TxB2** was infused into the pulmonary circulation of isolated perfused rat lungs. The metabolites were analysed from the nonrecirculating perfusion effluent. When the lungs were ventilated with cigarette smoke the amount of unmetabolized **TxB2** in the effluent was increased by 50%. The amount of the main metabolite was, however, not changed. The efflux of radioactivity from the lungs after a bolus injection of 3H-**TxB2** was slower during cigarette smoke ventilation than during air ventilation. This suggests that cigarette smoke inhibits the enzymes metabolizing **TxB2** rather than the pulmonary thromboxane uptake system.

268: J Assoc Physicians India 1983 Sep;31(9):573-5
Effect of prolonged smoking and alcohol on lipid profile, separately and in combination.

Baldwa VS, Gupta MC, Maheshwari VD, Bhansali A

269: Acta Paediatr Scand 1983 Sep;72(5):755-6
Lipoprotein pattern in umbilical cord blood of neonates of smoking and non smoking mothers.

Mau G, Brinkmann G, Anger H

PM3000457488

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

270: Arteriosclerosis 1983 May-Jun;3(3):273-81
Factors associated with lipoprotein cholesterol levels. The Framingham study.

Wilson PW, Garrison RJ, Abbott RD, Castelli WP

Lipoprotein cholesterol determinations in 6328 individuals aged 20 to 79 years in the Framingham Heart Study Cohort and Offspring were related by multiple regression analysis to reported cigarette **smoking**, alcohol intake, and Quetelet Index (wt/ht2). Cigarette **smoking** was found to be strongly associated with "atherogenic" lipoprotein cholesterol profiles in young adults, and particularly in women. The associations for alcohol intake were mostly uniform across age groups and lipoprotein cholesterol fractions, while coefficients for Quetelet Index varied considerably. Blood chemistry associations were studied in participants under 50 years, after controlling for **smoking**, Quetelet Index, and alcohol intake. Significant associations for high density lipoprotein cholesterol (**HDL**-C) were seen for both sexes with alkaline phosphatase, serum calcium, serum u ric acid, and leucocyte count. Low density lipoprotein cholesterol (**LDL**-C) associations were observed with calcium, hematocrit, lactate dehydrogenase, and leucocyte count in men and women, while very low density lipoprotein cholesterol (V**LDL**-C) associations occurred with alkaline phosphatase, glucose, uric acid, and leucocyte count in both sexes. A 1 mg/dl higher calcium corresponded to an **HDL**-C approximately 4 mg/dl greater and a **LDL**-C typically 6 mg/dl greater after controlling for 12 other variables. A 1000/ml increase in leucocyte count was typically associated with a decrease in **HDL**-C by 1 mg/dl and an increase in **LDL**-C and V**LDL**-C of 1 mg/dl each.

271: Adv Prostaglandin Thromboxane Leukot Res 1983;11:359-64
Acute effect of cigarette smoking on cardiac prostaglandin synthesis and platelet behavior in patients with coronary heart disease.

van der Giessen WJ, Serruys PW, Stoel I, Hugenholtz PG, de Leeuw PW, van Vliet HH, Deckmyn H, Vermylen J

PM3000457489

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

272: Prostaglandins Leukot Med 1982 Aug;9(2):141-50
Effects of smoking on platelets and on plasma thromboxane-prostacyclin balance in man.

Mehta P, Mehta J

To determine the influence of brief period of **smoking** on platelet release and platelet-vessel wall prostaglandins, we studied 13 non-smokers and 15 habitual smokers. Blood samples were collected before and immediately after **smoking**. Before **smoking** plasma beta-thromboglobulin levels were similar in the two groups. Plasma levels of **thromboxane B2** (**TXB2**), stable metabolite of TXA2 were slightly higher (124 +/- 43 vs 101 +/- 36 pg/ml) and of 6-keto-PGF1 alpha (stable metabolite of PGI2) lower (39 +/- 23 vs 63 +/- 23 pg/ml) in smokers compared to non-smokers. Immediately after **smoking**, plasma **TXB2** levels increased 197% (P less than 0.05) and plasma 6-keto-PGF1 alpha 44% (P-NS) in non-smokers. Similar increases were not observed in the smoker population, although plasma beta-thromboglobulin levels increased 40%. Platelet TXA2 generations induced by arachidonic acid and thrombin were similar in the two groups. These data show that brief period of **smoking** stimulates both TXA2 and PGI2 release in the non-smokers. Increase in TXA2 is more than in PGI2. Episodic increase in TXA2 may be a mechanism of vascular injury. Absence of increase in TXA2 and PGI2 with **smoking** in habitual smokers may reflect tolerance to effects of **smoking**.

273: Circulation 1982 Jul;66(1):44-8
Plasma catecholamines, platelet aggregation and associated thromboxane formation after physical exercise, smoking or norepinephrine infusion.

Siess W, Lorenz R, Roth P, Weber PC

To study the possible role of catecholamines in platelet activation, platelet aggregation stimulated by ADP, collagen, arachidonic acid and L-epinephrine, **thromboxane B2** (**TXB2**) formation and plasma levels of catecholamines and renin were studied in healthy men both before and after 6 days of propranolol treatment (40 mg three times daily) under control conditions and during sympathoadrenergic stimulation by physical exercise (200 W) or **smoking**. Exercise markedly increased plasma norepinephrine from 128 +/- 28 to 998 +/- 418 pg/ml (+/- SD), and plasma renin activity from 1.0 +/- 0.5 to 4.2 +/- 1.8 ng AI/ml . hour. **Smoking** predominantly increased plasma epinephrine, from 47 +/- 25 to 154 +/- 76 pg/ml. Propranolol did not consistently influence these variables, but blunted the circulatory response to exercise and **smoking**. Despite the marked increases of plasma catecholamines after both stimuli with and without beta blockade, platelet aggregation stimulated by ADP, 1-epinephrine, collagen and arachidonic acid and associated **TXB2** formation were not enhanced. Moreover, as already suggested by a trend toward reduced aggregability in these settings, plasma norepinephrine levels in the same range (745 +/- 368 pg/ml) due to infusion (5 micrograms/min) significantly reduced platelet aggregation with low-dose collagen (0.25-0.75 micrograms/ml), I-epinephrine (0.2-1.0 microM) and ADP (0.5-1.5 microM). These data do not support a role of endogenous catecholamines in initiating platelet activation and **TXB2** formation.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

274: Med Biol 1982 Jun;60(3):144-8

Effect of LDL from smokers and non-smokers on cell mass, proliferation, and collagen secretion by rabbit smooth muscle cells and human skin fibroblasts in culture.

Stavenow L, Kjellstrom T, Malmquist J

The effects of **low density lipoproteins** (**LDL**) from non-smokers and heavy smokers on rabbit aortic smooth muscle cells and human skin fibroblasts in culture were studied. The addition of **LDL** in increasing concentrations resulted in a decrease in cell mass. When data correction for cell loss was made, collagen secretion and cell proliferation were found to have been increased by **LDL**. The two different cell types used did not differ in their response to **LDL**. The effect of **LDL** from smokers and non-smokers was the same. Thus there was no indication of growth stimulation by factors carried by **LDL** from smokers, i.e. lipid-soluble hydro-carbons--mutagens.

275: Prev Med 1982 Jan;11(1):1-12
Smoking, oral contraceptives, and serum lipid and lipoprotein levels in youths.

Voors AW, Srinivasan SR, Hunter SM, Webber LS, Sklov MC, Berenson GS

276: Am Rev Respir Dis 1981 Oct;124(4):397-401
Human alveolar macrophages: a lesion in arachidonic acid metabolism in cigarette smokers.

Laviolette M, Chang J, Newcombe DS

Human pulmonary macrophages (PAM) recovered from young cigarette smokers and from age- and sex-matched subjects who had never smoked were used to investigate arachidonic acid metabolism. The uptake of radiolabeled arachidonic acid by PAM obtained from smokers and nonsmokers was not significantly different. The phagocytic indexes of the smoker and nonsmoker macrophages were 17.4 X 3.9% and 18.5 +/- 5.0%, respectively. Both smoker and nonsmoker macrophages produced prostaglandin E2 (PGE2), **thromboxane B2** (**TXB2**) and **prostaglandin F2 alpha** (**PGF2** alpha). A significant decrease in PGE2 and **TXB2** synthesis but not in **PGF2** alpha synthesis by the smoker PAM compared PAM compared with the nonsmoker PAM was observed using 2 different assays to measure prostaglandin production. Nonsmoker macrophages produced 644 +/- 128,239 +/- 53, and 29 +/- 12 ng/1.5 X 10(6) cells of PGE2, **TXB2**, and **PGF2** alpha, respectively, whereas smoker macrophages synthesized 168 +/- 20, 41 +/- 3, and 17 +/- 1 ng/1.5 X 10(6) cells, as measured by radioimmunoassay. Similar differences were observed using isotopic assays. A cigarette-smoke-induced lesion in phospholipid hydrolysis or the mechanism regulating phospholipid hydrolysis seem most consistent with these findings.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

277: Arteriosclerosis 1981 Jan-Feb;1(1):13-24
Levels and interrelationships of serum and lipoprotein cholesterol and triglycerides. Association with adiposity and the consumption of ethanol, tobacco, and beverages containing caffeine.

Phillips NR, Havel RJ, Kane JP

We have carried out a cross-sectional multivariate analysis of serum and lipoprotein lipid levels in white persons from an industrial population. Very low density lipoprotein triglyceride level was independent of ethanol consumption but increased with adiposity and cigarette **smoking** and decreased with coffee-tea drinking. Concomitant age variation in indices of adiposity accounted for only a small part of the sex-specific age trends in triglyceride level. Very low density lipoprotein cholesterol level was independent of all variables considered when controlled for very low density lipoprotein triglyceride. **Low density lipoprotein** cholesterol covaried with very low density lipoprotein triglyceride among normotriglyceridemic persons. Small increases in **low density lipoprotein** cholesterol level with adiposity and cigarette **smoking** appeared to reflect associated increases in very low density lipoprotein triglyceride. Increased **low density lipoprotein** cholesterol level with age, however, was largely independent of concomitant age variation in very low density lipoprotein triglyceride. **High density lipoprotein** cholesterol level increased with ethanol consumption and decreased with adiposity and cigarette **smoking** even after adjustment for its inverse relationship with very low density lipoprotein triglyceride.

278: Am J Clin Nutr 1980 Dec;33(12):2581-7
Adiposity, lipids, alcohol consumption, smoking, and gender.

Sutherland WH, Temple WA, Nye ER, Herbison GP

Indices of obesity, plasma lipids, and lipoprotein levels, plasma cholesteryl ester fatty acid composition, reported alcohol consumption and **smoking** habits were measured in 88 men and 87 women, ages over 15 years, randomly selected from the total respondents (1192) to a health survey. Most indices of obesity were related to plasma triglycerides and **high-density lipoprotein** levels in both sexes; to very low-density lipoprotein levels in men only; and to plasma cholesteryl ester fatty acid linoleic acid proportions in women only. The correlations with **high-density lipoprotein** cholesterol levels were dependent on very low-density lipoprotein triglyceride levels in men but not in women. Indices of obesity were significantly higher in non**smoking** women and reported alcohol consumption correlated with Quetelet's index (body mass index) in men. **Smoking** habits, but not alcohol consumption, influenced correlations between indices of obesity and plasma triglycerides and very low-density lipoprotein triglyceride levels in men. The present results showed several sex-related differences in relationships with indices of obesity. Lower very low-density lipoprotein levels, higher skinfold measurements, higher cholesteryl ester fatty acid linoleic acid proportions and lower alcohol intake in women than in men may be responsible. The data suggested that in women, altered diet composition may be linked with obesity.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

279: Pol Tyg Lek 1980 Oct 20;35(42):1599-601
[Effect of smoking on blood serum concentration of total cholesterol and cholesterol of lipoprotein fractions].

[Article in Polish]

Kapuscinska B, Bochenek W, Chwistecki K

280: Circulation 1980 Jun;61(6):1188-93
Atherosclerosis-related responses to cigarette smoking in the baboon.

Rogers WR, Bass RL 3d, Johnson DE, Kruski AW, McMahan CA, Montiel MM, Mott GE,
Wilbur RL, McGill HC Jr

Thirty-six young adult male baboons (Papio cynocephalus) were fed an atherogenic diet (40% calories from lard, 1.5 mg cholesterol/kcal) and taught to puff by operant conditioning with water rewards. Eighteen baboons (smokers) were assigned randomly to smoke 43 cigarettes a day, and 18 baboons (shams) were assigned randomly to puff air under conditions equivalent to those of the experimental group. During months 14-19 of **smoking**, cigarette-**smoking** baboons had significantly higher carbon monoxide and thiocyanate concentrations in blood and cotinine concentrations in urine. There were no significant differences in serum total cholesterol, V**LDL** + **LDL** cholesterol, **HDL** cholesterol or triglyceride concentrations of smokers and shams. **Smoking** baboons had significantly higher fasting blood glucose concentrations and lymphocyte counts. Platelet count, platelet aggregation, food and water intake, and body weight were not significantly different in the two groups.

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

281: Circulation 1979 Jul;60(1):22-5
The combined effect of smoking and coffee drinking on LDL and HDL cholesterol.

Heyden S, Heiss G, Manegold C, Tyroler HA, Hames CG, Bartel AG, Cooper G

Conflicting reports on the effect of **smoking** and coffee drinking on lipoproteins prompted us to study the combined effect of these two associated, widely prevalent habits in 361 persons randomly sampled from the Evans County cohort. Low-density lipoprotein (**LDL**) cholesterol levels were significantly higher among persons who smoked cigarettes and consumed five or more cups of coffee per day than among nonsmokers who abstained from coffee. Conversely, high-density lipoprotein (**HDL**) cholesterol was higher in persons who did not smoke or drink coffee than in coffee-consuming smokers. However, this trend was not statistically significant. Triglycerides and very low-density lipoprotein (**VLDL**) cholesterol were highest among smokers who drank five or more cups of coffee per day, but these differences did not reach statistical significance. Lipoprotein cholesterol levels were adjusted for age, sex and body mass. **Smoking** and coffee drinking interact in affecting **LDL** and total cholesterol, but coffee drinking alone did not appear to affect blood lipids.

282: Rev Invest Clin 1978 Oct-Dec;30(4):367-8
Serum concentration of alfa-2HS glycoprotein, prealbumin, beta-lipoprotein, alfa-1-antitrypsin and IgG in healthy smokers.

Rostenberg I, Navarrete C, Arredondo F, Herrera R, Guizar-Vazquez J

283: Ann N Y Acad Sci 1978 Mar 30;304:128-39
Hypertension, blood lipids, and cigarette smoking as co-risk factors for coronary heart disease.

Kannel WB

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001

284: Lancet 1977 Dec 24-31;2(8052-8053):1327-8
Peripheral vascular disease in cigarette smokers and impaired hepatic metabolism of lipoprotein remnants.

Topping DL, Dwyer T, Weller RA

The metabolism of very-low-density lipoproteins and chylomicrons includes the extrahepatic hydrolysis of their triglycerides by lipoprotein lipase. This results in cholesterol-rich "remnants" which are further metabolised by the liver. There is experimental evidence that in both patients with type-III hyperlipoproteinaemia and cigarette smokers hepatic-remnant metabolism may be depressed. In type-III hyperlipoproteinaemia the defect is inherited while in smokers it occurs in response to raised blood concentrations of carboxyhaemoglobin. The striking clinical similarity between type-III hyperlipoproteinaemic patients and smokers--namely, a high incidence of peripheral vascular disease--may be due to a common cause, the accumulation of cholesterol-rich remnants in the plasma.

285: Arch Pathol 1974 Dec;98(6):418-21
Cigarette smoking and cholesterol atherosclerosis of rabbits.

Fisher ER, Wholey M, Shoemaker R

PM3000457495

Source: https://www.industrydocuments.ucsf.edu/docs/plcl0001